Marc H. M. Hermans
UEMS Vice-President

12 February, 2020

Dear Dr. Hermans,

Here please find our report:

According to the general UEMS viewpoints about the Multidisciplinary Joint Committees (MJC), a primary aim of them is to certify the highest standards of education for physicians and other learners in order to promote patient safety, they aim to advance the science of clinical education, training, and assessment in a multidisciplinary manner in sections with mutual interest on the field of the MJC. The MJC aims to create a system of support for the delivery of state of the art clinical skills training within the European Union (EU) and EU affiliated countries in the UEMS area.

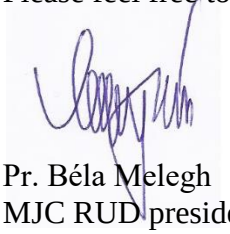
Keeping these general messages in mind, the Section of Clinical Genetics contacted the presidents and secretaries of the sections (Appendix 1.), then proposed the creation (Appendix 2.) of the MJC of Rare and Undiagnosed Disease (MJC RUD); the proposal was discussed and approved at the Warsaw Council meeting of the UEMS, by a 100% support of the voting nations.

The kickoff meeting (Appendix 3.) was executed in association of the UEMS Council meeting in Brussels, 2016. The delegates decided about the bureau modality (Appendix 4.); the MJC RUD will be governed under the umbrella of the Section of the Clinical Genetics (https://clinicalgenetics-uems.pte.hu/). The kickoff meeting of the MJC RUD was addressed by Enrique Terol (Appendix 5.), Policy Officer of European Commission, ERN coordinator. The MJC RUD strategic plans included operational partnership with the UEMS sections and MJCs, and in boarder context, with the launched European Reference Networks as well.

After the kick off meeting the following gatherings took place:

- Unofficial meeting in Vilnius, Lithuania (Appendix 6. and 7.)
- Conference Presentation by Dr. Melegh (Appendix 8.)
- MJC RUD Meeting in Brussels 2018 (Appendix 9. 10. and 11.)
- Unofficial meeting in association with London council meeting (No official report)
- Memorandum of Understanding documents (Appendix 12. and 13.)
- Further attached documents are the ETR's submitted to the 2020 council meeting. (Appendix 14.)
- Annual report 2019 (Appendix 15.)

Please feel free to contact me if any additional information is needed.



Pr. Béla Melegh
MJC RUD president

Appendix 1

Dear UEMS Sections Presidents and Secretaries,

The purpose of this letter is to seek partners in the task of a joint approach in drafting the goals of a newly formed MJC, the "Rare and Undiagnosed Diseases" Committee.

Rare disease have been attracting special attention for the last decade, and we are now at the start of a new era, hopefully a rewarding 'golden age', largely brought about by the introduction of game-changing new genetic technologies, namely whole exome and genome sequencing, following on from the progress achieved through various forms of array technology.

Among humankind there are some 6,000-8,000 rare diseases, some of them being relative common and well known, while others are extremely rare. The term "Diagnostic Odyssey" has been coined to describe numerous such patients who circulate in the non-harmonized labyrinths of various branches of medicine.

Most of these rare diseases have a genetic basis; therefore we, as clinical geneticists, frequently coordinate care and play a kind of harmonizing role in the management of these patients, fully aware that a multidisciplinary approach is needed, and that many, if not all subspecialties within the medical professions make a significant contribution to this important task.

Our goal is to establish the MJC of "Rare and Undiagnosed Diseases", as this daily, fast-moving area also has clear educational consequences that should be harmonized. We, the Clinical Genetics section of the UEMS, will be proposing the creation of this MJC in the forthcoming Warsaw meeting. We are ready and willing to receive any suggestions or comments you may have, up to the end of July. Please also let us know if you have suggestions for any position or volunteering role – this would be welcome. To keep to the schedule, we then have until mid-August to finalize our supporting evidence and credentials the Sections who are actively participating, with the final submission of materials to the UEMS SG due by the end of August.

Yours sincerely,

Ulf Kristoffersson
Past-President

Bela Melegh
President

6.1. *Proposed creation of a MJC Rare and Undiagnosed Diseases ***

This item was proposed by UEMS Section of Clinical Genetics

Béla Melegh
president
UEMS Council meeting
16-17th October, 2015
Warsaw

Appendix 2

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
SECTION OF CLINICAL GENETICS

Dr Edwin Borman
Secretary General
Union Européenne des Médecins Spécialistes
European Union of Medical Specialists
Rue de l'Industrie, 24
1040 – BRUSSELS

25 August, 2015

Dear Professor Borman,
Dear Secretary General,

On behalf of the Clinical Genetics section (CGS) of the UEMS, hereby I contact you with the request to create an MJC for "Rare & Undiagnosed Diseases". Attached please find a short summary to underline the rationale of this action, with the list of sections of the UEMS in annex who already expressed their interest. Please put into the agenda of Warsaw meeting this aim to enable us to present the objectives to the National Representatives and to the representatives of the sections.

Yours sincerely,

Béla Melegh
president of CGS

Mailing Address:
University of Pécs, Department of Medical Genetics
H-7624 Pécs, Szigeti út 12.
Hungary
Tel.: (+36) 72 536 427; Fax: (+36) 72 536 032

Establishment of UEMS MJC for "Rare and Undiagnosed diseases"

Background, specific challenge:
In most of the EU countries a disease considered as rare (or orphan) disease if the disease affect not more than 5 per 10 000 persons in the general population. This group, however, is quite large, as it is estimated that rare diseases include about 6 000 to 8 000 separate entities, affect altogether more than 30 million people in the EU countries. It was already recognized, that due to the small and dispersed patient populations of the individual specific rare diseases the international collaborations in the diagnosis, care, treatment, and research efforts are crucial. The rare disease task recently has been modified and the task extended to include the whole spectrum of the undiagnosed diseases as well. This task involves most if not all medical specialties. About 80-90% of this disease group has genetic background, about 10-15% is non-genetic amongst the non-communicable part, and 5-10% has infectious origin. Thanks to advances of the new tools like the array technology and the next generation sequencing, great progress is seen in the understanding the molecular pathogenesis of the diseases of genetic origin, the research and the diagnosis is tightly linked in this field. Albeit the European Commission recognized the significance of this issue, and numerous huge systemic research projects have been granted, moreover, the implementation of European Reference Network for rare diseases is now on the way, almost any step towards a systemic and harmonized EU compatible training scheme has been devoted.

Scope:
The aim of this effort includes the incorporation of the principles of methods of genomics and/or other –omics and/or other high-throughput approaches used in the molecular characterization of rare and undiagnosed diseases into the training of medical experts of various sub-specialties. As the undiagnosed rare diseases may range from groups of disorders with relatively common and phenotypically well described diseases to groups of diseases with extremely rare incidence rate an almost unknown molecular basis, care should be taken to the appropriate training of the experts about common standards and terminologies for rare disease classification and also support their training on appropriate bioinformatics tools and incentives to facilitate data sharing, including the management of the existing resources used for depositing data generated by the different platforms.

Expected impact:

- Provide better understanding of genomic methods for the correct diagnosis of undiagnosed rare diseases for which there is no or unsatisfactory diagnosis available.
- Contribute thereby towards the multidisciplinary harmonization of the essential knowledge base of the new generation genomic approaches.
- Foster dissemination of novel scientific results and knowledge exchange between specialties.
- Provide better knowledge for improved family counselling as well as to improve follow-up for patients.
- Help to develop knowledge management strategies, with the view of facilitating models of care and access to the data gathered by different rare disease networks.
- Help putting into the right practice on the EC regulations on the *in vitro* diagnostic medical devices, with special focus on the genetic diagnostic ones.
- Contribute to the development of the best practice to regulate how and by whom patients are counselled before a genetic test.

Type of action: MJC

The goals related to this topic are optimally provided by the MJC conditions. The MJC proposal should enable and foster exchange between stakeholders from countries and regions with different practices and strategies of rare disease task.

Interest of UEMS Sections & Boards about creation of the Rare and Undiagnosed Diseases MJC:

Founder:
Section of Clinical Genetics, Bela Melegh
Charter members:
Section of Internal Medicine, Reinold Gans
Section of Medical Oncology, Serdar Turhal
Section of Child and Adolescent Psychiatry, Dame Sue Bailey
Section of Dermatology and Venereology, Magdalena Czarnecka-Operacz
Section of Infectious Diseases, Jean-Paul Stahl
Section of Pediatric Surgery, Gian Battista Parigi
Section of Neurology, Patrick Kras

Personal: Giorgio Berchicci, and Helena Alves (Section of Laboratory Medicine)

Appendix 3

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS

Association internationale sans but lucratif *International non-profit organisation*

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS MJC Rare and Undiagnosed Disease

Kick-off Meeting of the MJC Rare and Undiagnosed Diseases

20 October 2016

1. Welcome address and introduction to UEMS Rules of procedures – Prof. Papalois
2. Election of the Bureau of the Section
3. Future activities of the Section, possible goals of MJC RUD – Prof. Melegh
4. European Reference Networks – Dr. Terol, European Commission
5. Next meeting
6. Any Other Business

Appendix 4

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS

Association internationale sans but lucratif — *International non-profit organisation*

AVENUE DE LA COURONNE, 20
BE- 1050 BRUSSELS
www.uems.net

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.net

UEMS MJC
RARE AND UNDIAGNOSED DISEASES

Minutes of the Kick-off Meeting of the MJC Rare and Undiagnosed Diseases (MJC-RUD)

20th October 2016, Brussels, Belgium

Motto: "Communication – Quality – Clinics"

Present:
Alexandre Bisdorff, Luxemburg
Nursel Calik Basaran, Turkey
Nada Cikes, Croatia
Rijk Gans, Netherlands
Marc Hermans, Belgium, UEMS
Daniela Karall, Austria
Ulf Kristoffersson, Sweden
Norbert Lukan,
Patrick Magennis, UK
Jaime Medrano, Spain
Bela Melegh, Hungary, President
Udo Rolle, Germany
Liesbeth Siderius, Netherlands
Grazyna Slaveta, Poland
Enrique Terol, Spain
Aivars Vetra, Latvia
Lotte Welinder, Denmark
Kristiina Aittomäki, Finland, Secretary

At the beginning of the meeting Prof. Melegh gave a short presentation on UEMS and its important role in educational harmonization in Europe. He also informed the participants that Prof. Papalois was unable to attend.

1. The meeting was officially opened by Prof. Marc Hermans, who attended the meeting as the representative of UEMS. The delegates introduced themselves.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

UEMS MJC
RARE AND UNDIAGNOSED DISEASES

2. The agenda that had been circulated to the registered participant was approved.

3. Professor Hermans introduced the UEMS Rules of Procedures (ROP) on multidisciplinary joint committees. The purpose of the bureau of MJC is to coordinate actions, circulate information, and prepare documents for the MJC. More information can be found on the UEMS website under Explanatory notes.

4. Election of the Bureau for the Multiple Joint Committee. Every MJC needs to have a bureau of at least two officials, President and Secretary. There was one candidate for both positions from the Section of Clinical Genetics, the President Professor Bela Melegh from Hungary and the Secretary Professor Kristiina Aittomaki.

   Professor Melegh was elected as the President and Professor Aittomaki as the Seretary to the MJC-RUD.

5. Future activities of the Section, possible goals of MJC RUD

   Prof. Melegh gave an introduction to the discussion. He noted that many European projects include educational packages, but at the end of these projects often very little has been done to actually enhance professional education. Furthermore, professional training on rare and undiagnosed diseases is presently weak. As high-quality education is one of the aims for the UEMS, the MJC-RUD could aim at enhancing training on rare and undiagnosed diseases. The strength of the MJC-RUD is that it includes many specialities and can reinforce any produced documents on the European level through UEMS Council meetings. He also encouraged all delegates to participate in the discussion on the aims of MJC-RUD.

   There was a lively discussion on the problems on how to deal with the multitude of rare diseases. It was noted that future doctors need expert skills in IT. Although much information is available also for the patients in the internet, we need capable specialists between the patient and Doctor Google and European harmonization to improve patient care. It was also noted that within the MJC-RUD it is possible to discuss and share both problems and experiences and that would benefit educational development.

   Professor Hermans pointed out that there are three central items to consider (in bold): You need **communication** to improve the **quality** of care in the **clinic**.

   One of the important goals for the MJC-RUD is to create awareness of the ERNs, when they are working, and to give advice to patients and doctors how to contact them.

6. Introduction to the present state of European Reference Networks by Dr. Enrique Terol, Policy Officer of European Commission

   Copies of Dr Terol's presentation will be circulated.

   Short notes from the meeting:
   ERNs have a legal base in European Union legal structure. Presently there are 24 applications for ERNs including 18-77 centres. Almost all countries have recognised the ERNs. The idea is not to establish networks for individual diseases, as hundreds of ERNs cannot be created, but broader thematic networks.

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

ERNS are a new environment of health care as they deal with patients that cannot be dealt with in their national health care and therefore need international healthcare. The idea, however, is that patients do not travel, knowledge travels. This arises questions such as "how do we incorporate this within national healthcare systems" and "how to organize nationally the flow of patients". The treatment of patients should preferentially be organized on national level. While the ERNs can give advice on how and where the patients should be treated, the member states can approve or deny their suggestions.

Questions to Dr Terol:

As the patients have overlapping symptoms, do the ERNs work together?
Meetings of the coordinators of the ERNs are organized and they are discussing on how they can work together on complex clinical situations. E-health platform is a possibility for interactions.

Do the ERNs treat the patient?
Basically the ERNs offer virtual health care, but they are included within the cross-border healthcare directive.

How can the MJC-RUD work with the ERNs?
MJC-RUD could have a very important role as an advisory body, introduce tools for any approach for patients or diseases, work on other areas such as training.

ERNs could ask us to help them rather than us intruding within their area.
We could perhaps participate in the meeting of coordinators to explain what the MJC-RUD is doing. Both parties should know what each does, goals and overlapping areas. In general, MJC-RUD should develop a document to explain what we are doing to other organizations working in the field of Rare and Undiagnosed Diseases**.**

7. Future meetings of the MJC-RUD will be organized in association with UEMS meetings. Between the meetings the participants will keep in touch via "group email".

8. A group photo of delegates was taken and the meeting was closed at 11.25

Brussels October 21, 2016

Kristiina Aittomäki, Secretary

European Reference Networks

European Commission

European Reference Networks

Directive of patients' rights in cross-border healthcare

Enrique Terol
DG SANTE
Directorate B
European Commission

Health and Consumers

European Commission

From concept to reality…our state of readiness

- ⇨ *Background and legal base*
- ⇨ *The ERN model*
- ⇨ *State of play of the ERN call*
- ⇨ *The way forward*

European Commission

The road to ERNs

European Reference Networks

Scope and Context

European Commission

Chapter IV Cooperation between MS
Article 12 European Reference Networks

Networks of healthcare providers aiming at

Improving quality and safety and access to highly specialised healthcare

✓**Patients affected by rare or low prevalence and complex diseases**

✓**multidisciplinary approach (different specialities/areas of knowledge)**

✓**Added value at EU level**

✓**Need of cooperation:**

- **Scarcity knowledge**
- **Need education**
- **Complexity / high cost**
- **Effectiveness in the use of resources**

The ERN model

European Commission

- *based in innovation*
- *a new way of understanding healthcare provision and knowledge generation*

European Commission

The bricks

Quality
High specialisation
Expertise
Knowledge
Research
Clinical care

The glue

Innovation
Trust
Solidarity
Generosity
Common project
eHealth

The goals & benefits

- ⇨Better care & Diagnosis
- ⇨Equal access
- ⇨Reduce clinical variation
- ⇨Develop standards
- ⇨New treatments
- ⇨Knowledge travels
- ⇨Generate evidence
- ⇨Better data
- ⇨Capacity building
- ⇨Economy of scale

Legal acts on ERN

What

17.5.2014 EN Official Journal of the European Union L 147/71

COMMISSION DELEGATED DECISION

of 10 March 2014

setting out criteria and conditions that European Reference Networks and healthcare providers wishing to join a European Reference Network must fulfil

(Text with EEA relevance)

(2014/286/EU)

17.5.2014 EN Official Journal of the European Union L 147/79

COMMISSION IMPLEMENTING DECISION

of 10 March 2014

setting out criteria for establishing and evaluating European Reference Networks and their Members and for facilitating the exchange of information and expertise on establishing and evaluating such Networks

(Text with EEA relevance)

(2014/287/EU)

How

Entry into force 27 May 2014

Appendix 5

Networks criteria and capacities

- ✓ knowledge and **expertise to diagnose, follow up and manage patients**
- ✓ Evidence of **good outcomes**
- ✓ **multi-disciplinary** approach
- ✓ capacity to **produce good practice guidelines and to implement outcome measures and quality control**
- ✓ **Research, teaching and training**
- ✓ collaborate with **other centers of expertise and networks**

European Commission

Key features of the Networks

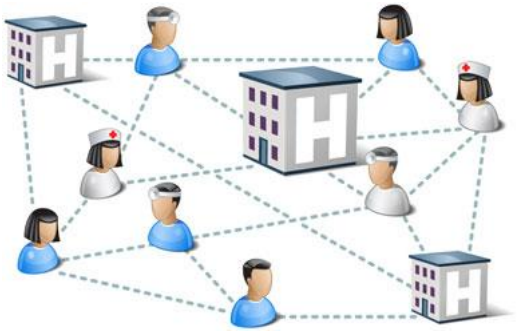
- ✓ *Patient centered and clinically lead*
- ✓ *10 Members in at least 8 Countries*
- ✓ *Strong independent (3rd party) assessment*
- ✓ *Fulfillment of Network and Members criteria*
- ✓ *Endorsement and approval by National Authorities (grouping and strategic value)*

Networks Governance

European Commission

- ✓ ***Transparent and effective*** *coordination & governance*
- ✓ ***Flexibility*** *and* ***key organizational features.***

European Reference Network



Board of the Network

Network Coordinator

Centre Representative

Centre Representative

Collaborative National Centre

Associated National Centre

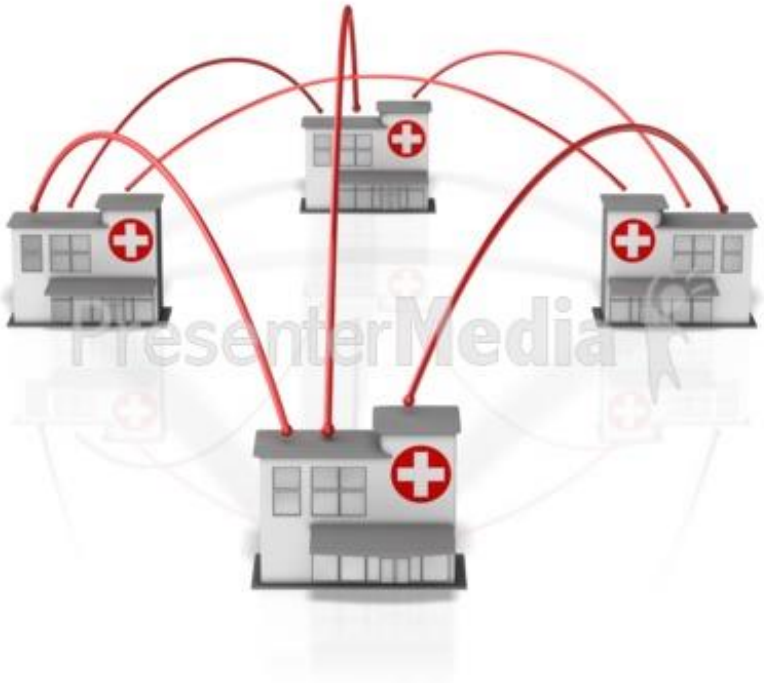
Scientific Societies

Patients Organisations

Academy

Other stakeholders

European Commission



Networks

Hospital

Experts units

European Commission

Key role of Member States

- ✓ **Recognition of centers at national level.** (important differences) MS with systems in place (minority)
- ✓ **Endorsement** of applications
- ✓ **Board of Member States**
- ✓ **Approval** of Networks (once positively assessed)

Terminology scope players

European Commission

National: competences

Health care providers

Healthcare System

Endorsement of application by MS

Centres Expertise/reference

National hubs
Collaborative Associated Centres

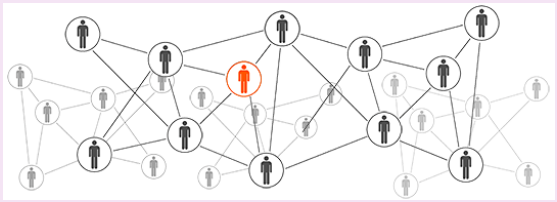
Cooperation – coordination at national level

EU level

Positive assessment

European Reference Network

Members of the Network



Special relation with the network

EU level

- No external assessment
- Designated by MS

Health and Consumers

European Reference Networks

Appendix 5

Challenges and Sucessess

European Commission

Integration

Breacking down the silos

Building bridges

- *Separated groups,*
- *Different pilot networks*
- *Different specialities,*
- *Lack of patient involvement,*
- *Lack of common standards, guidelines, information…*

European Commission

Mayor challenge

Thematic groups

Shared position of Commission Expert group on Rare Diseases, Member States and Patients associations

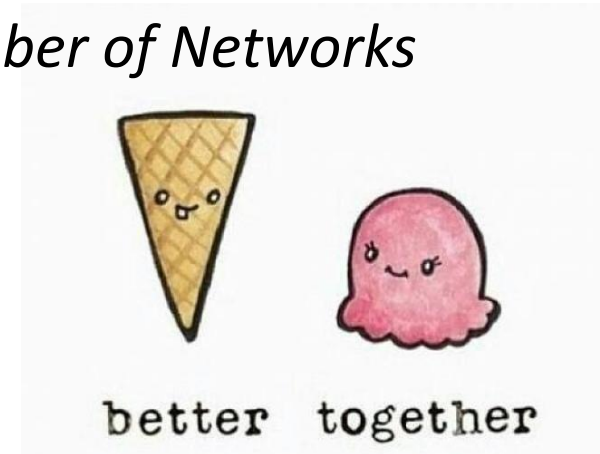
***Rational**: Avoid fragmentation and overlapping*

***Pros:** Strategic approach: manageable number of Networks*

All diseases will find a "home"

Integrative and seamless approach

Multidisciplinarity



***Contras:** complexity of governance, time to find agreements, different "ecosystem" & resistance to change*

European Commission

Call for ERN

March - July 2016

Health and Consumers

European Reference Networks

Appendix 5

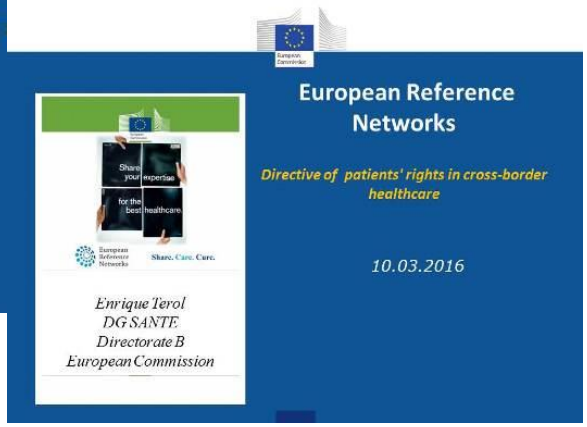
Communication & awareness activities

European Commission

Info Day

ERN Info day 7th April

Third European Union Action Programme in the field of Health - National Focal Points Meeting 18th March



Health and Consumers

European Reference Networks

European Commission

Update on the ERNs calls (1st and 2nd wave)

- ✓ **24** Network proposals
- ✓ **370** hospitals
- ✓ **960** expert units involved
- ✓ **26** Countries (25 EU Member States plus Norway)
- ✓ Covering **major challenges** in rare and complex diseases and conditions
- ✓ **20 thematic areas** included in the proposal of the Expert Group on Rare diseases (Gynaecology only partially)

Appendix 5

Remember… (3)

European Commission

2013:

HAS DECIDED AS FOLLOWS:

Article 1

European Reference Network

To apply for registration of European Reference Networks (ERN) logo as a trade mark in the EU, Norway, Iceland, Liechtenstein and Switzerland in the name of the European Union, and in relation to the abovementioned services.

Done at Brussels, 16.10.2013

For the Commission
Paola Testori Coggi

European Commission

Sustenability and Support to the ERNs

European Reference Networks

⇨ **Health Programme <u>2016</u>**

- Grants to support networking activities
- Patient registries projects
- Technical assistance assessment ERNs applications
- 3rd ERN Conference (March 2017) Kick off meeting ERNs

⇨ **Connecting European Facilities (2015-2017)**

- IT Platform

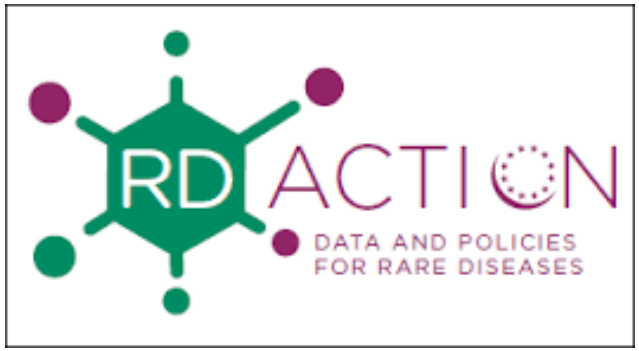
European Commission

Research Programme H2020 and potential future actions on Rare Diseases Research.

European Reference Networks

European Commission

Join Action on Rare Diseases:



Appendix 5

ERN tentative timeline & milestones

European Commission

July 2016

Call for Networks

July-November 2016

Assessment proposals

December 2016

Approval ERN by Board MS

November 2016 – March 2017

Grant evaluation

March 2017

3rd ERN Conference & Kickoff meeting ERNs

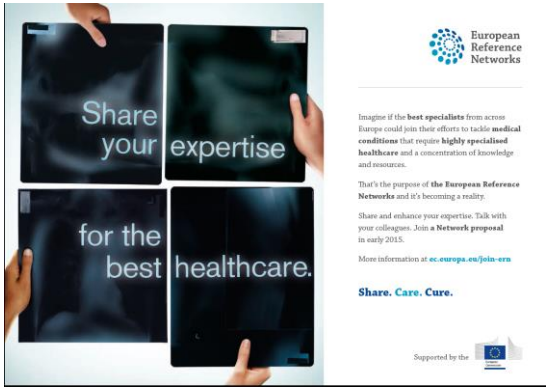
Health and Consumers

European Reference Networks

European Commission

Thank you!

European Reference Networks



http://ec.europa.eu/health/ern/policy/index_en.htm

SANTE-ERN@ec.europa.eu

Enrique.terol@ec.europa.eu
Helene.LE-BORGNE@ec.europa.eu
Anna.carta@ec.europa.eu

Appendix 6

UEMS MJC

Rare and Undiagnosed Diseases

Informal meeting March 8th 2017, Vilnius, Litouania

Present:

Bela Melegh, President, Hungary

Liesbeth Siderius, Acting Secretary, Netherlands

Ulf Kristofferson, Sweden

Alessandre Renieri, Italy

Arunas Valiulis, Litouania part present

1. General discussion:

There is still unclearness about the quality assessment of the national expert centres.

Each country has different registration systems. For example Sweden has a large register with nu specific registration of rare diseases. EuroGenTest is a good example of qualification of genetic laboratory tests. At present there is no funding to continue.

In pediatrics rare diseases are common practice of most subspecialities. Pediatric training includes training in subspecialities and thus in the murtidisciplinary care of the child with a rare disease. In Hungary the person with a rare disease living in rural area remains out of sight of specialist care. Italy has coordination of rare diseases is in public health by regions which all report to the national health.

The MJC RUD is a commission of the UEMS, proposed by the clinical genetic society and adopted by all UEMS members.

How is the MJC financed? There is no budget.

Do we need a website? Maybe UEMS MCJ's tab or other, no strategy jet.

2. *Suggestions formulated as goal:*

The UEMS sets standards for high quality healthcare practice that are transmitted to the Authorities and Institutions of the EU and the National Medical Associations. An UEMS Multidisciplinary Joint Committee addresses a field of a multidisciplinary nature.

The MJC RUD is established to bridge the gap between medical specialist societies and to facilitate high quality multidisciplinary care for the persons with a rare or undiagnosed condition.

MJC RUD has identified steps in the frame of the establishment of 24 European Reference Networks:

- harmonization of a common core training in principles of rare diseases (such as early recognition, access to diagnostic test, multidisciplinary care and societal expectations)
- provide CME accredited training programs at conferences and by E learning

3. The MJC RUD needs some financial support: in the first place for travel and accommodation. Suggestions made EU/ ERN's, a project, UEMS

4. During the ERN conference March9th Bela had a short conversation with Enrique Terol (Policy Officer of European Commission). Enrique welcomed the suggestion of a common core straining.

5. Actions:
-The draft as noted will be send to all MJC RUD members.
-There will be another informal meeting in Tel Aviv.
-We will have a room at the EURORDIS meeting in Budapest: May 19-21.
-Invite all ERN coordinators at the MJC RUD October meeting in Brussles.

LS March 12th 2017

Appendix 7

Dr Enrique Terol
Policy Officer
SANCO – D2 Healthcare Systems
European Commission

Re.: Collaboration between the Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases (MJC-RUD) of UEMS and the European Reference Networks Coordinators Group (ERN CG)

Dear Dr. Terol, dear Enrique,

As you know, the European Union of Medical Specialists (UEMS) aims to improve standards for high quality healthcare practice in order to support the Authorities and Institutions of the EU as well as the National Medical Associations. Within the UEMS, Multidisciplinary Joint Committees (MJCs) address areas which are of a professional multidisciplinary nature. The MJC for Rare and Undiagnosed Diseases, the MJC-RUD, was established in 2016 to bridge the gap between medical specialist societies and to facilitate high quality multidisciplinary diagnosis and care for people with rare or undiagnosed conditions.

European Reference Networks (ERNs) are expected to improve the care for patients with rare diseases. Therefore, the MJC-RUD welcomes the 24 newly established European Reference Networks. The ERNs are established in frame of the directive cross boarder health care, Directive 2011/24/EU. The directive defines a health professional as a doctor of medicine, a nurse responsible for general care, a dental practitioner, a midwife or a pharmacist within the meaning of Directive 2005/36/EC. With the experience that exists within UEMS with regard to setting training standards, developing syllabi, developing teaching materials and setting criteria for assessment by the different medical societies, we propose to build a structural collaboration between the MJC-RUD and the ERN's.

Specifically, there are two important issues where we could work together with the 24 European Reference Networks:

- provide of a common core training principles of rare diseases for MJC RUD participating medical specialties with the help of the ERN CG, and ultimately with the individual education working groups later;
- collaborate in EACCME CME accredited training programs both on site like courses and conferences and by e-learning, as the EACCME of the UEMS is the main EU scientific event accreditation body.

As a first step, we would contact the leaders of the ERN CG asking their willingness about partnering in specialist training within the ERN CG framework issues "Knowledge generation: Training, education, capacity building; guidelines development" task package. Later, when this partnership already established, we would more specify the necessary further steps.

Currently, several medical disciplines within the UEMS already offer specialist training in rare diseases. Therefore, we are also interested to learn how the leaders of the 24 ERNs envisage to contribute to these existing training programs. Specifically, as rare diseases disproportionally affect children, we are

looking forward to your thoughts about how we can ensure that their specific needs are also addressed in future training programs.

We hope you find our offer useful and look forward for a possible collaboration to improve health care for European citizens with rare disorders, and will support our initiative.

With best personal regards,

Bela Melegh, MD, PhD
Professor
Chair UEMS Section for Clinical Genetics
Chair UEMS MJD for Rare and Undiagnosed Diseases

Appendix 7

ERN Coordinators Group
"Knowledge generation:
Training, education, capacity building; guidelines development"
Specific tasks group

Dear Colleagues,

On behalf of the Multidisciplinary Joint Committee on Rare and Undiagnosed Diseases (MJC RUD) of the European Union of Medical Specialists (UEMS) we congratulate to your continuous efforts lead to the successful launch of the European Reference Network (ERN) system. We believe, that this is a real milestone in the rare disease management in Europe.

As you may know, the main goals of the UEMS, the oldest and biggest medical society in Europe, includes the harmonization of the training. The UEMS, via the EACCME, the ratified accreditation body for training programs like on-site courses, e-learning events, or conferences, plays a central role in the continuing medical education (CME) in Europe.

The MJC RUD is a recently formed working group of the UEMS. The primary goal of it is to implement the UEMS general and specific goals for the rare disease fields, to make a knowledge based bridge between the different medical sections of the UEMS, representing basic pillars of the European medical specialist training.

All of the 24 ERNs have education working groups. We propose establishment a long-term partnership between us, therefore we would appreciate if you could joint to this ERN-MJC RUD Partnering initiative. Please inform us if your ERN is open is development of education resources, including education and training modules, programs, or e-learning modules that you are aware of.

Yours sincerely,

Béla Melegh, MD, PhD
professor
President of MJC RUD

UEMS as a wide communication platform for the ERN activities, transfer of knowledge and training achievements towards the entire European community of medical specialists

RD-ACTION & DG Sante Workshop. 6-7 December, 2017 – Rome

Béla Melegh
[1]Department of Medical Genetics, University of Pécs, Hungary
[2]Section of Clinical Genetics, & [3]Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases of the European Union of Medical Specialist (UEMS)

Appendix 8

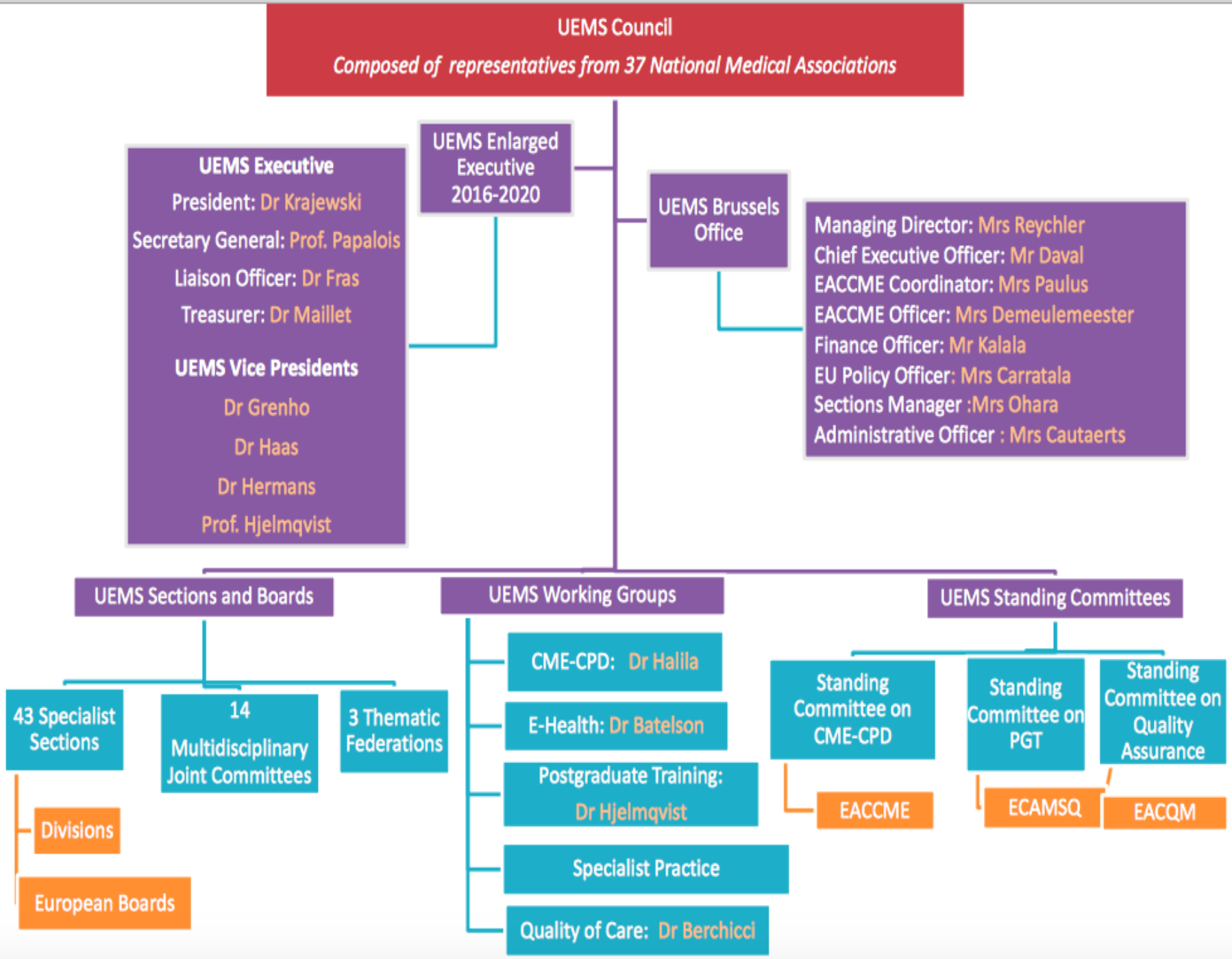
I. The UEMS

European Union of Medical Specialists (established in 1958)

info@uems.eu

Appendix 8

https://www.uems.eu/__data/assets/pdf_file/0014/21353/UEMS-Organogram-March-2016.pdf



WHO ARE WE?

Full Members

- National Medical Associations of the 28 EU Member States & of the 3 European Economic Area Countries

Other members

- 3 Associate Members: Armenia, Israel &Turkey
- 3 Observers: Georgia, Lebanon, Morrocco

GENERAL ASSEMBLY:
The "UEMS Council"
37 National Associations of Medical Specialists

Appendix 8

UEMS STRUCTURE

Council's Missions :

- **Setting** and **promoting** high quality Training and medical practice standards
- **Representating** of Specialists
- **Advocating** of Professional interests

GENERAL ASSEMBLY:
37 National Associations of Medical Specialists
Representing 1.6 million specialists

Executive's Missions :

Implement the Council's decisions
Represent UEMS at EU level
Ensure smooth running of UEMS
Maintain close relations with UEMS Bodies

UEMS Executive

UEMS Bodies

- 43 Specialist Sections
- 14 Multidisciplinary Joint Committees
- 3 Thematic Federations
- European Boards
- Divisions

Working Groups

- CME-CPD
- E-health
- Postgraduate training
- Specialist Practice & Quality of Care

Standing Committees

- CME-CPD
  - EACCME
- Postgraduate training
  - ECAMSQ
- Quality Assurance

Appendix 8

Sections

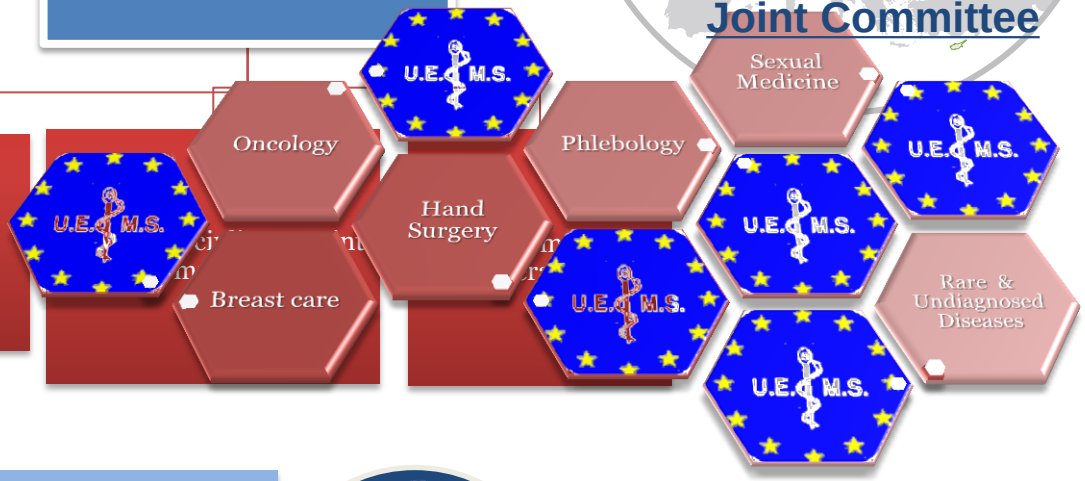
- Emergency Medicine
- Endocrinology
- Gastroenterology
- Geriatrics
- Gynaecology & Obstetrics
- Infectious Diseases
- Internal Medicine
- Ophthalmol
- Surgery
- Radiolog
- Cardiology
- Clinical pharmacology
- Psychiatry
- Neurology
- Pathology
- Rhematology
- Clinical Genetics

43 **Specialist Sections** & European Boards
21 **divisions** within Sections
14 **Multidisciplinary Joint Committees**
3 thematic federations

Multidisciplinary Joint Committee

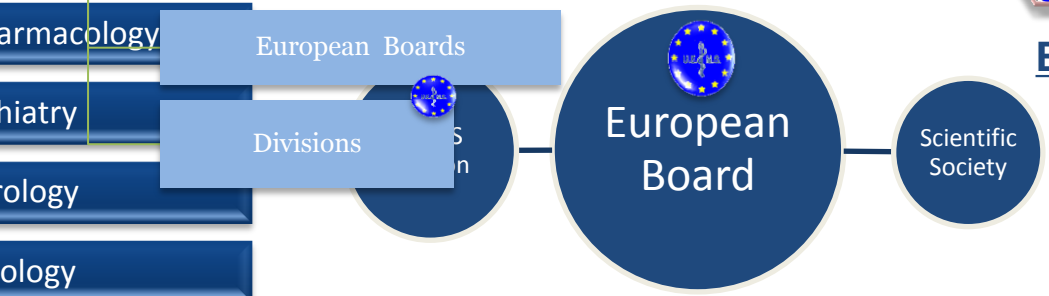
UEMS Bodies

43 Specialist Sections



European Boards

Divisions



European Board

Role :
Specialty Representation & standards setting

CME-CPD

Postgraduate training

Quality Assurance

UEMS ACTIVITIES 1

Specialist Accreditation

- *Setting t*
- *Advocati*
- *Developi* *petence*

Subm

- *Organ* *ed in USA &*

www.eaccme.eu

EU AFFAIRS

Involvement as expert in

- Commission's Joint Action on Healthcare Workforce
- Study on Effective Recruitment and Retention strategies
- Directive Professional qualifications
- EU-funded projects
  - E-Health
  - Data Protection
  - European Reference Networks
- Other Stakeholders
  - Medical Industry : Medtech (code of ethic in PGT)

Appendix 8

II. The European Accreditaion of events: The EACCME

info@uems.eu

The European Accreditation Council for CME (EACCME®)

Under the impulse of a growing shift from voluntary to mandatory CME-CPD in Europe, the European Union of Medical Specialists (UEMS) set up the European Accreditation Council for Continuing Medical Education (EACCME®) in October 1999.

The UEMS-EACCME® began its activities in January 2000 with the mutual recognition of accreditation of EU-wide and international CME-CPD activities for live educational events through the awarding of European CME credits (ECMECs) to individual medical specialists, allowing the recognition and exchange of CME credits between all European countries.

In April 2009 the UEMS-EACCME® launched the accreditation of e-learning materials. By e-learning is meant the delivery of CME-CPD by methods including: recorded audio, recorded visual, recorded

eaccme.uems.eu

Apple iCloud Bing Google Wikipedia Facebook Twitter Időkép TripAdvisor Blog EACCME OTP Bank Outlook TeveClub! UDN EACCME UEMS BitTorrent ESHG Gmail Gige_hid

EACCME

Technical support | All other questions Help

THE EUROPEAN ACCREDITATION COUNCIL FOR CONTINUING MEDICAL EDUCATION

INSTITUTION OF THE UEMS

Home Accredited events Accreditation Library LOGIN

Welcome, bmelegh .

logout

Register

Please register if you have not received a login yet.

I am a provider

III. NEW EACCME GOALS:

« Development of a training module for reviewers »

info@uems.eu

EACCME working group Development of a training module for reviewers
29 July 2017

Appendix 8

IV. Postgraduate training: NASCE (Network of Accredited Skill Centers in Europe)

info@uems.eu

Appendix 8

About NASCE

The Network of Accredited Clinical Skills Centres in Europe (NASCE) is established as a Multidisciplinary Joint Committee (MJC) of the Union Européenne des Médecins Spécialistes (UEMS) and follows UEMS statutes, rules and directives. It is open to members of any Section of the UEMS wishing to participate. The Sections are participating in the MJC as equal partners.

Objectives

The Multidisciplinary Joint Committee manages the interests of NASCE and promotes individual, inter-professional and multidisciplinary clinical skills education. The primary aim is to certify the highest standards of education for surgeons, physicians and other learners in order to promote patient safety. In addition to that the MJC aims to advance the science of clinical education, training, and assessment.

NASCE - Home

Members Area | Contact | English

NETWORK OF ACCREDITED SKILLS CENTRES IN EUROPE

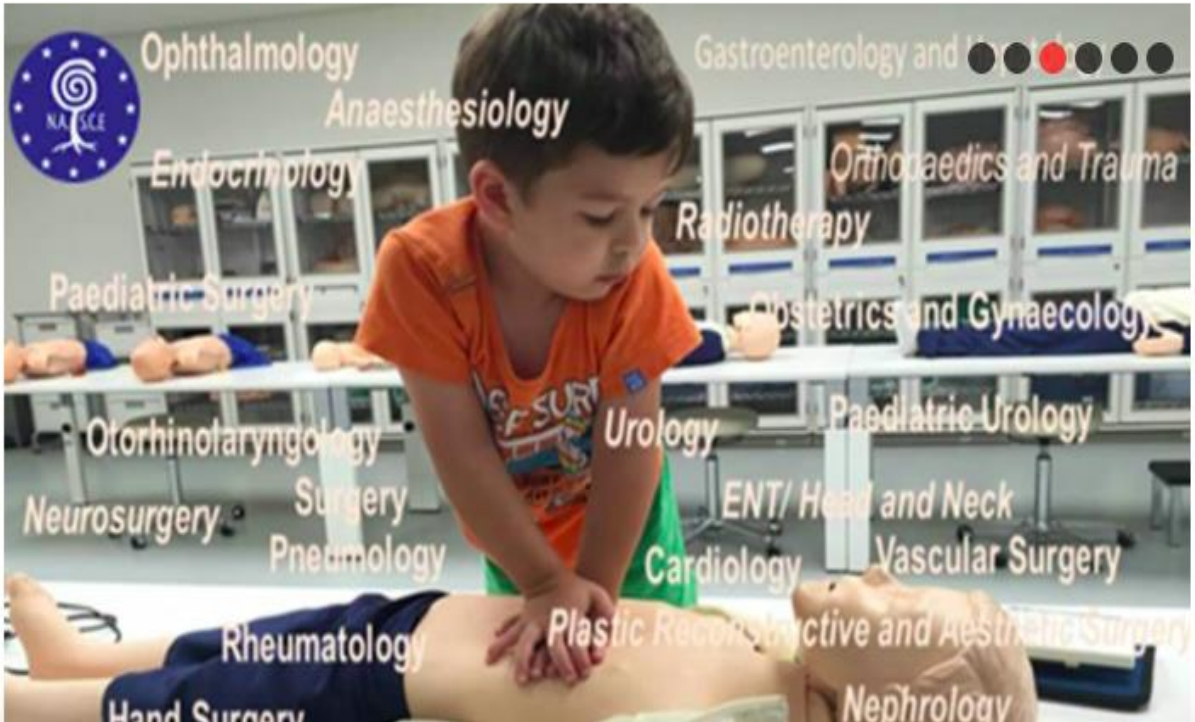
Structure Accreditation News & Events Accredited centers Gallery Registration

NASCE - Home

Members Area | Contact | English

NETWORK OF ACCREDITED SKILLS CENTRES IN EUROPE

Structure Accreditation News & Events Accredited centers Gallery Registration



Appendix 8

V. Postgraduate training: CESMA (Council for European Specialits Medical Assessment) The EU Exams

info@uems.eu

Areas of Expertise

CME - CPD

Postgraduate Training

European Standards in Medical Training - ETRs

Competence-Based training and assessment

CESMA

CESMA Appraisals

CESMA Meetings

CESMA Meeting Glasgow

The Council for European Specialists Medical Assessment

The CESMA is an advisory body of the UEMS created in 2007 with an aim to provide recommendation and advice on the organisation of European examinations for medical specialists at the European level.

It was called in the beginning the "Glasgow group" referring to the first meeting held in Glasgow. It was then decided to adopt the name CESME (Council of European Specialist Medical Examinations). This name was finally changed to CESMA (Council of European Specialist Medical Assessment)

Its main role is to:

- To promote harmonisation of European Board assessments
- To provide guidelines to the Boards on the conduct of assessments
- To encourage take up of Board assessments as a quality mark
- To offer an alternative to National assessments, where appropriate

Appendix 8

1., ETR (UEMS 2017/06)

General arrangement; 12 pages; special care on skills and competencies; Clinical and laboratory; 4/5 yrs of training

2., Description of Clinical Genetics as a Medical Specialty in EU (UEMS 2017/06A)

Revision of the 2009 yrs UEMS document; (6 pages)

3., Syllabus (UEMS 2017/06/B)

18 pages; 5 Domains: 1. Theoretical genetics / Basic science; 2. Clinical/Medical knowledge and specialist-level skills; 3. Genetic counselling and communication skills; 4. Laboratory skills; 5. Ancillary competences

Existing EU Exams

1. Allergology and Clinical Immunology
2. Anesthesiology
3. Cardiology
4. Dermatology & Venereology
5. Otorhinolaryingology
6. Hand Surgery
7. Intensive Care
8. Internal Medicine
9. Neurology
10. Neurosurgery
11. Nuclear Medicine
12. Ophthalmology
13. Oromaxillofacial Surgery
14. Orthopaedics and Traumatology
15. Pathology
16. Pediatric Surgery
17. Physical and Rehabilitation Medicine
18. Plastic, Reconstructive and Aesthetic Surgery
19. Radiology
20. Respiratory Medicine
21. Surgery (General Surgery)
22. Coloproctology
23. Endocrine Surgery
24. Surgical Oncology
25. Thoracic Surgery
26. Transplantation
27. Trauma Surgery
28. Thoracic and Cardiovascular Surgery
29. Urology
30. Vascular Surgery
31. Angiology
32. Emergency Medicine

Appendix 8

VI. MJC RUD:
MULTIDISCIPLINARY JOINT COMMETTEE
OF
RARE AND UNDIAGNOSED DISEASES

info@uems.eu

Appendix 8

Kickoff meeting of Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases (MJC RUD); European Union of Medical Specialties (UEMS). Brussels, 20th October, 2016

Appendix 8

VII. Examles for the early steps: Partnering with the JARC

info@uems.eu

the Joint Action on Rare Cancers

FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI
UNIVERSITÀ DEGLI STUDI DI MILANO

Paolo G. Casali
paolo.casali@istitutotumori.mi.it

JARC
JOINT ACTION ON RARE CANCERS

Objectives

With regard to RCs in the EU, to improve:

1. **Epidemiological surveillance**
2. **Quality of care through ERNs**
3. **Clinical practice guidelines**
4. **Innovation**
5. **Medical and Patient education**
6. **Health policy measures**
7. **Patient empowerement**

Work packages

WP		
1	Coordination	
2	Dissemination	A, GR
3	Evaluation	CSF, FI
4	Epidemiology	INT, IT
5	Assuring Quali	OECI
6	Clinical p nes	DKG, DE
7	Inn ccess to innovation	WIV-ISP, BE
8	ication	UP, HU
	mood Cancers	SIOPE
	Rare Cancer Policy	ICO, ES

Patient empowerement

ECPC, EURORDIS, CCI E

Objectives

1. **using data of WP6**, **to delineate optimal resources for undergraduate medical education,** including paediatric oncology, that fits the European training requirements and standards; **to identify the educational resources available in Europe for post-graduate medical education**, with attention to those European regions where outcomes are statistically poorer;
2. to identify optimal ways and approaches to **connect the educational resources** available throughout Europe **with networked health care**, with special regard to **ERNs;**
3. **to promote the improvement** of European medical expert training instruments **via the European Union of Medical Specialists (UEMS), as well as SIOPE – European Society for Paediatric Oncology,** where paediatric oncology is concerned;
4. to provide recommendations on education of **non-medical experts, patient advocates and patient communities** involved in patient care, as a means to improve rare cancer patient empowerment in Europe.

Appendix 8

Meeting notes: Joint Action for Rare Cancers & GENTURIS ERN

28 September 2017

Attendees:	Matt Bolz-Johnson, EURORDIS (Chair)
	Nicoline Hoogerbrugge, GENTURIS ERN Network Coordinator
	Nicoline Geverink, GENTURIS Network Manager
	Paolo Casali, Joint Action for Rare Cancer Lead
	Annalisa Trama, Joint Action for Rare Cancer Lead
	Bela Melegh, GENTURIS & JARC
	Ariane Weinman, EURORDIS
Apologies:	Claas Röhl, GENTURIS ePAG

- **2. Meeting objectives**
- The aim of the meeting was:
- Secure a detailed understanding of the scope and activities of GENTURIS European Reference Network (ERN) and the Joint Action for Rare Cancers (JARC).
- To explore the potential areas of collaboration between GENTURIS ERN and the JARC.

5. JARC & GENTRUIS Potential Areas of Collaboration

Collaboration Aims:

- **5.1 Clinical Practice Guidelines**
- **5.2 Training & Education**
- **5.3 Policy Areas**

5.3 Training & Education

- Bela Melegh was identified as the education and training lead that ‘bridge’ GENTURIS and the JARC. He agreed to coordinate the education and training activities between the 3 RC ERNs, GENTURIS and the JARC.
- **Action**: BM to coordinate medical education and training between the JARC and the 3 RC ERNs & GENTURIS.

Action Points

No.	Action	Lead
1.	JARC leads & GENTURIS agreed to identify experts working under initiative and to connect these experts up.	ALL
2.	To share the priority list of CPGs and the clinical leads with GENTUIRS.	PC
3.	To identify expertise in GENTURIS who can liaise with JARC clinical leads on the CPG.	NH
4.	To share rare cancers list with GENTURIS	AT
5.	Bela to coordinate medical education and training between the JARC and the 3 RC ERNs & GENTURIS.	B

Appendix 8

JOINT ACTION ON RARE CANCERS

Joint Action on Rare Cancers - Survey on Medical Education for Undergraduates and Postgraduates

1. Basics

Within the framework of Joint Action on Rare Cancer (http://jointactionrarecancers.eu/) WP8 you are invited to participate in the following survey. Our goal is to collect data on the education and training programs currently available for under- and postgraduates related to the rare cancers, including childhood cancers. In the present survey the current classification of the rare cancers is the reference material:

1. Head and neck cancers (cancers of nasal cavity and sinuses, nasopharynx, hypopharynx, larynx, salivary glands, oropharynx, oral cavity and lip, eye, middle ear)
2. Thoracic rare cancers (tumours of trachea, thymus, malignant mesothelioma)
3. Male genital and urogenital rare cancers (tumours of testis, penis, renal pelvis, ureter, urethra and extragonodal germ cell tumours)
4. Female genital rare cancers (tumours of vulva and vagina, non epithelial tumours of ovary, trophoblastic tumours of the placenta)
5. Neuroendocrine tumours
6. Tumours of the endocrine organs (cancers of thyroid, parathyroid, adrenal cortex, pituitary gland)
7. Central Nervous System tumours (Glial tumours, medulloblastoma, malignant meningioma)
8. Sarcomas (sort tissue sarcomas, bone sarcomas, gastrointestinal stromal tumours)
9. Digestive rare cancers (Tumours of small intestine, anal canal, gallbladder and extrahepatic biliary duct)
10. Rare skin cancers and non-cutaneous melanoma (melanoma of mucosae and of the uvea, adnexal skin carcinomas, Kaposi sarcoma)
11. Haematological rare malignancies (acute myeloid leukemia, myeloproliferative neoplasms, myelodisplastic and myeloproliferative neoplasms, histiocytic and dendritic cell neoplasms)
12. Pediatric cancers (all pediatric cancers are considered as rare cancers)

JOINT ACTION ON RARE CANCERS

NEXT

Page 1 of 4

Never submit passwords through Google Forms.

Appendix 8

JOINT ACTION ON RARE CANCERS

Joint Action on Rare Cancers - Survey on Medical Education for Undergraduates and Postgraduates

3. Undergraduate Training

7. Are you involved in the training of medical students?
- Yes
- No

8. Does your department have specially dedicated undergraduate training course on rare cancers?
- Yes
- No

9. To you knowledge, does your department have special teaching materials for rare cancer training of undergraduates?
- Yes
- No

10. In general, how can your knowledge and awareness of the rare cancers be characterized?
- Poor
- Acceptable
- Well informed

11. In general, how can the knowledge and awareness of other training personnel in your institution about the rare cancers be characterized?
- Poor
- Acceptable
- Well informed

12. In general, how can the knowledge and awareness of the training personnel in your country about the rare cancers be characterized?
- Poor
- Acceptable
- Well informed

13. Please evaluate the contribution of the individual disciplines to the rare cancer training.

	1 - Poor	2 - Acceptable	3 - Excellent	4 - Not applicable
Biophysics	○	○	○	○
Molecular Cell Biology	○	○	○	○
Behavioural Science	○	○	○	○
Medical Chemistry	○	○	○	○
Anatomy	○	○	○	○
Biochemistry	○	○	○	○
Pharmacology	○	○	○	○
Pathophysiology	○	○	○	○
Microbiology	○	○	○	○
Dermatology	○	○	○	○
Otolaryngology	○	○	○	○
Internal Medicine	○	○	○	○
Clinical Biochemistry	○	○	○	○
Clinical Radiology	○	○	○	○
Public Health	○	○	○	○
Oncology	○	○	○	○
Oral Medicine	○	○	○	○
Orthopaedics	○	○	○	○
Urology	○	○	○	○
Surgery	○	○	○	○
Traumatology	○	○	○	○
Paediatrics	○	○	○	○
Neurology	○	○	○	○
Psychiatry	○	○	○	○
Obstetrics and Gynaecology	○	○	○	○
Ophthalmology	○	○	○	○
Anaesthesia and intensive care	○	○	○	○
Family Medicine	○	○	○	○
Medical Genetics	○	○	○	○
Psychiatry	○	○	○	○

14. Which disciplines should definitely enhance their performance in the rare cancer training?

	1 - Not at all	2 - Moderately	3 - Strongly	4 - Not applicable
Biophysics	○	○	○	○
Molecular Cell Biology	○	○	○	○
Behavioural Science	○	○	○	○
Medical Chemistry	○	○	○	○
Anatomy	○	○	○	○
Biochemistry	○	○	○	○
Pharmacology	○	○	○	○
Pathophysiology	○	○	○	○
Microbiology	○	○	○	○
Dermatology	○	○	○	○
Otolaryngology	○	○	○	○
Internal Medicine	○	○	○	○
Clinical Biochemistry	○	○	○	○
Clinical Radiology	○	○	○	○
Public Health	○	○	○	○
Oncology	○	○	○	○
Oral Medicine	○	○	○	○
Orthopaedics	○	○	○	○
Urology	○	○	○	○
Surgery	○	○	○	○
Traumatology	○	○	○	○
Paediatrics	○	○	○	○
Neurology	○	○	○	○
Psychiatry	○	○	○	○
Obstetrics and Gynaecology	○	○	○	○
Ophthalmology	○	○	○	○
Anaesthesia and intensive care	○	○	○	○
Family Medicine	○	○	○	○
Medical Genetics	○	○	○	○
Psychiatry	○	○	○	○

15. How can the knowledge and awareness of the new MD graduates about the rare cancers be characterized?
- Well informed
- Acceptable
- Poor

16. To your knowledge how fragmented is the European training in undergraduate level comparing the nations?
- Very fragmented
- Medium fragmented
- Well-harmonized
- Do not know

17. Do you see rationale in the pan-European harmonization of the training?
- Disagree
- Agree
- Strongly agree
- Do not know

BACK NEXT Page 3 of 4

Never submit passwords through Google Forms.

JOINT ACTION ON RARE CANCERS

Appendix 8

1., ETR (UEMS 2017/06)

General arrangement; 12 pages; special care on skills and competencies; Clinical and laboratory; 4/5 yrs of training

2., Description of Clinical Genetics as a Medical Specialty in EU (UEMS 2017/06A)

Revision of the 2009 yrs UEMS document; (6 pages)

3., Syllabus (UEMS 2017/06/B)

18 pages; 5 Domains: 1. Theoretical genetics / Basic science; 2. Clinical/Medical knowledge and specialist-level skills; 3. Genetic counselling and communication skills; 4. Laboratory skills; 5. Ancillary competences

Appendix 8

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS2017/06B

Syllabus for residents and trainees in Clinical Genetics

This syllabus is an outline and flexible summary of major and specific topics to be covered in some way in the training course of a resident. The basic goal of the syllabus is to help and ensure a fair and impartial understanding between the instructor and students such that there is minimal confusion in the topics, setting clear expectations of material to be learned. The syllabus provides neither a roadmap of course, nor organization/direction relaying the instructor's teaching philosophy to the trainees, as the syllabus is not a learning guide. Rather, the syllabus is a supporting reference material, content and priorities of training may vary in different training institutions.

Domain 1: Theoretical genetics / Basic science

1.1 Cellular and molecular mechanisms that underpin human inheritance

1.1.1 Basics
- 1.1.1.1 Nucleic acid structure, DNA and RNAs
- 1.1.1.2 Translation, protein structure
- 1.1.1.3 Chromosome structure and function (ploididty and cell cycle)
- 1.1.1.4 Monogenic vs. multifactorial inheritance
- 1.1.1.5 Mutations, variants, CNV
- 1.1.1.6 Cells, cell proliferation, cell specialization
- 1.1.1.7 Nuclear and mitochondrial genome
- 1.1.1.8 Gene editing, CRISPR

Appendix 8

2.13.4 Cancer genetics

- 2.13.4.1 Be able to take a relevant history, perform an appropriate examination and undertake risk estimation using a variety of methods
- 2.13.4.2 Use of cancer registers and other sources to verify diagnoses
- 2.13.4.3 Use disease registers to support follow-up of affected and at-risk patients
- 2.13.4.4 Assessment of screening protocols for at-risk relatives
- 2.13.4.5 Identify at-risk patients and relatives who are eligible to participate in trials of cancer prevention strategies
- 2.13.4.6 Rare cancers; differences and similarities with rare diseases. Types (classification: Pediatric cancers, Haematologic rare neoplasms; Sarcomas; Rare thoracic cancers; Neuroendocrine tumours; Head & neck cancers; Central nervous system tumours; Rare female genital cancers; Rare urological and male genital tumours; Endocrine gland tumours; Digestive rare cancers; Rare skin cancers & non-cutaneous melanoma)

2.13.5 Reproductive genetics

- 2.13.5.1 Be able to provide preconceptional genetic counselling to couples with sub-/infertility and organize genetic testing
- 2.13.5.2 Be able to provide preconceptional genetic counselling to couples with genetic and inherited disorders for their reproductive choices including invasive diagnosis, non-invasive testing, and assisted reproductive technologies (ART)
- 2.13.5.3 Be able to inform on the different ART options according to the national legislation and European guidelines including preimplantation genetic testing

2.13.6 Skeletal Genetics

- 2.13.6.1 Be able to formulate a differential diagnosis of a fetus suspected of having a skeletal dysplasia or dysostosis and assess whether the condition is compatible with postnatal survival
- 2.13.6.2 Be able to formulate a differential diagnosis for a child with a congenital limb, axial, and/or craniofacial malformation, including teratogenic causes, syndromic causes, and skeletal dysostoses/dysplasias
- 2.13.6.3 Be able to evaluate radiographs and other imaging studies and know when to order further biochemical or molecular genetic tests, as well as which tests are appropriate for a given situation

Appendix 8

Appendix 9

UEMS - EUROPEAN UNION OF MEDICAL SPECIALISTS

MULTIDISCIPLINARY JOINT COMMITTEE ON RARE AND UNDIAGNOSED DISEASES

MJC RUD Meeting
in association with the
UEMS Council Meeting
Saturday, 20th October, 2018.
12:00-13:00
Thon Brussels City Center
Avenue du Boulevard 17, 1210 Brussels,
Room "Sonja"

AGENDA

1. Welcome, approval of the Agenda
2. Annual report of the President
3. ENETS Proposal (Vassilios Papalois, UEMS Secretary General)
4. ETR for "Rare Diseases"
5. "European Board of Rare Diseases"
6. ETR for "Rare adult solid cancers"
7. "European Board of Rare adult solid cancers"
8. Joint Action on Rare Cancers (JARC) documents & activities (report)
9. Election of the Secretary
10. AOB

Appendix 10

UEMS - EUROPEAN UNION OF MEDICAL SPECIALISTS

MULTIDISCIPLINARY JOINT COMMITTEE ON RARE AND UNDIAGNOSED DISEASES

Minutes taken by LS & BM

Minutes of UEMS Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases (MJC RUD) board meeting

Date: October 20, 2018; 13:15-14:00			**Protocol No** 3/2018
Place: Thon Hotel, Brussels			
Attendees: Vassilios Papalois (special guest) *UEMS Secretary General* Bela Melegh *President, Section of Medical Genetics* Liesbeth Siderius *acting Secretary, Section of Pediatrics* Alexandre Bisdorff *Section of Neurology* Serdar Ceylander *Turkish NMA* Maeve Durkan *Section of Endocrinology* Marc Hermans *Section of Psychiatry* Norbert Mulleneisen *Section of Allerology* Apologies: Marisa Dias Nursel Celik Basaran Daniela Karall			

Appendix 10

	Points	**Discussion**	**Decisions**	
1	Opening	Meeting is open at 13:15, with delay.	Due to the delay, the Agenda points 2 & 8 to be discussed mainly electronically, points 4-7 to be discussed together verbatim	BM
2	Agenda point 3	ENETS contacted the UEMS for collaborate in EU exam. A confcall was organized (04.07.18) with A. Pascher, A. Frilling, VP, Lise Carratala, BM. ETR materials were sent along to ENETS partners by LC. IT expert involvement to the MJC RUD suggested	MoU needs to be prepared soon (before their meeting in 30.11.18.) VP will send available MoU forms to BM; a Position (white) paper will be considered on “undiagnosed” topic. MJC RUD will find partners for collaboration via email contact of Sections	VP BM to be named BM
3	Agenda points 4-7	ETR for "Rare Diseses" European Board of Rare Diseases ETR for “Rare adult solid cancers” European Board of Rare adult solid cancers”	All points were considered merit for further development. Call will be circulated amongst Section to identify experts who interested to join; working group(s) will be created	BM
4	Agenda point 8	Joint Action in Rare Cancers (JARC)	Was incorporated in part into the previous point, slides will be circulated later.	BM
5	Agenda point 9	Election postponed (low number of attendees, lack of proxies)	LS remains acting secretary	VP, BM
6	AOB	MD & NM MJC RUD membership application was approved	Monetary support via EU grants will be considered	

Appendix 11

UEMS - EUROPEAN UNION OF MEDICAL SPECIALISTS

MULTIDISCIPLINARY JOINT COMMITTEE ON RARE AND UNDIAGNOSED DISEASES

Annual Report of the President – 2018

12 February, 2019

The calendar year of 2018 was the second full year in the history of the MJC RUD.

Membership

We had a total of 37 members from 11 Sections (OMF, IM, Ophthalmology, Paediatrics, Psychiatry, Rheumatology, Medical Genetics, Neurology, Paediatric Surgery, Pharmacology, and Rehabilitation. They represented 21 Countries, and of them 3 were non EU Nations (Armenia, Georgia, Turkey).

The Bureau

The Bureau consisted of the President and an acting Secretary.

Meetings

There was a membership meeting in Brussels UEMS Council Meeting; Saturday, 20th October, 2018.; 12:00-13:00 (Agenda and Minutes are attached)

Main focus in 2018 and after

See the Agenda and Minutes

Finances

During the year 2018 there was no budget or income of the MJC RUD. However, the president evaluated 6 life events for the CESMA.

Participation in other activities

Ulf Kristoffersson had an active role in the preparation of the EU Exam in Medical Genetics and Genomics in the Section of Medical Genetics. The president participated in the work of the EACCME "Training the reviewers" working group.

On behalf of the Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases:

Béla Melegh
President

Appendix 12

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif International non-profit organisation

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS 2019 / 20

MEMORANDUM OF UNDERSTANDING

BETWEEN:

1. **UEMS (European Union of Medical Specialists)**, an international non-for-profit organization incorporated under the laws of Belgium, having its registered seat at 24 rue de l'Industrie, 1040 Brussels – Belgium, acting through its Multidisciplinary Joint Committee of Rare and Undiagnosed Diseases [MJC RUD], hereby validly represented by;

   Hereafter: "UEMS"

   and

2. **European Neuroendocrine Tumor Society (ENETS) e.V.**, a Medical Society incorporated under the laws of Germany having its registered seat at Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum, Dept. of Hepatology and Gastroenterology, Augustenburger Platz 1, D-13353 Berlin, Germany,

   hereby validly represented by [Prof. Dermot O'Toole, ENETS chairman, and Prof. Bertram Wiedenmann, ENETS treasurer

   Hereafter: "European Society"

The parties sub (1) and (2) shall hereafter be referred to individually as a "Party" and collectively as the "Parties".

RECITALS

The UEMS and the European Society are active in areas relevant to the quality of medical specialist practice in Neuroendocrine Tumours in Europe and to the quality of care for the benefit of European patients. The Parties are willing to create a partnership that will promote and facilitate their activities in this area.

The overall goal of collaboration and cooperation is to define joint actions, to achieve the best possible outcomes and to increase visibility of both parties.

The parties seek through this Memorandum of Understanding ***("MoU")*** to define their partnership, to explore and to develop new opportunities in accordance with their objectives and competence. Through this MoU, the Parties also aim to establish an efficient and transparent communication between them.

THE PARTIES DECLARE THAT

1. **SCOPE**

This MoU outlines the principles of cooperation and collaboration between the UEMS Section and the European Society.

2. **INTENTION OF THE PARTIES**

The Parties acknowledge that this MoU does not, and is not meant to, constitute a legally binding agreement between them. Whenever an activity undertaken by both Parties would require a formal legal framework Parties will conclude a formal, legally binding agreement.

The non-binding relationship between the UEMS and the European Society governed by this MoU is that of independent contractors. Nothing contained in this document will be construed as constituting any other relationship between the Parties.

This MoU does not prevent or limit European Society or UEMS to enter agreements with other parties. Both Parties declare that they will not enter agreements that would jeopardize or invalidate this MoU and, whenever reasonable doubt would arise as to whether a new agreement is likely to be in conflict with this MoU, the Parties will communicate and strive to resolve outstanding issues.

3. **INTERNAL POLICIES**

Subject to the terms of this MoU, the implementation and pursuit of the goals, objectives, conditions and terms of this collaboration will be carried out in accordance with the internal policies and procedures of each Party.

4. **SCOPE OF COMPETENCES AND ROLES**

a) ***European Scientific Society***

According to its articles of association, the European Society mission is to

- improve the diagnosis and therapy of patients with neuroendocrine tumors in an international, interdisciplinary and scientific context
- coordinate research at European hospitals and health research institutes, with emphasis on basic and clinical research for the diagnosis and treatment of NETs
- further develop standards for the accreditations of ENETS Centers of Excellence
- offer education and training for physicians and scientists at annual scientific and educational meetings
- focus on writing and updating NET guidelines for all aspects of NET care including treatment and standards of care and subsequently publicising in medical and scientific journals
- foster the exchange of forums for young investigators
- support collaborative scientific projects of excellence
- communicate with and inform patient advocates and patient self-help groups
- cooperate with the pharmaceutical industry for the development of new diagnostic, therapeutic and information technologies
- further endorse the ENETS Registry and Centers of Excellence throughout Europe

To achieve this goal, the key activities of the European Society include:

- the promotion of basic research on neuroendocrine tumor diseases and innovative diagnostic and therapeutic procedures,
- the continuation of the hitherto successful cooperation between European Centers of Excellence,
- the promotion of young researchers and clinicians in the field of neuroendocrine tumor diseases,
- the promotion of research through the raising of funds and the establishment of endowed professorships,
- the promotion of science through the establishment of service areas,
- the promotion of research through the collective use of technical resources,
- the promotion of the dissemination of advancements in the medical treatment of neuroendocrine diseases and the protection of interests of affected patients and treating physicians,
- the promotion of the Europe-wide transfer of advancements in research and medical treatments into teaching and postgraduate training,
- the recognition and representation of mutual objectives of clinicians and basic researchers in this field.

b) UEMS

According to its articles of association, the UEMS objectives are to promote the harmonization of training standards for specialist physicians within the European Union and to promote free movement of specialist doctors within the European Union. The UEMS is independent from medical industry in order to assure unbiased position in areas of medical politics and in accreditation of CME.

5. MUTUAL RECOGNITION

Each Party acknowledges the competences of the other, according to its articles of association.

Each Party acknowledges that the other is an essential partner in the development and improvement of the quality of medical specialist practice of Diagnosis, Treatment and Aftercare of NEUROENDOCRINE TUMOURS in Europe. Parties recognize that their continued collaboration should be a crucial and integral element to the future success of both organizations and their members.

6. AREAS OF COOPERATION BETWEEN THE UEMS AND THE EUROPEAN SOCIETY

Parties undertake to collaborate in order to achieve the objectives of mutual interest.

The areas of collaboration between the UEMS and the European Society can include, but shall not be limited to:

- Elaboration of European specialist training curriculum
- Organisation of specialist European examinations
- Organisation of visitation programs
- Development and promotion of high quality, unbiased CME/CPD
- Setting European standards of specialist practice
- Provision of joint opinion and statements to the EU institutions

The UEMS and the European Society commit to working in close cooperation and to actively exchange information that is of common interest and/or might be of significance to both organizations and their members.

Parties recognize that:

- each Party is a key partner in areas of collaboration described in this document;
- European Society expertise concentrates on organization of CME/CPD, scientific research, development of practice guidelines and standards,
- UEMS expertise concentrates on accreditation of CME/CPD, elaboration of Training Requirements and curricula and organization of European Examinations.

Parties agree to involve the other Party when elaborating major policy documents at the earliest possible stage of the process in order to receive its input.

7. COMMUNICATION

The MJC RUD will be responsible of communication with the European Society in all matters regarding areas of cooperation defined in this MoU, including communications to the UEMS Executive, other UEMS bodies and to UEMS constituency. This MoU does not change the UEMS representation rules described in statutory documents or waive information and approval duties of MJC RUD.

The European Society will communicate with UEMS Section in all matters regarding areas of cooperation defined in this MoU.

The European Society and the MJC RUD will each appoint a person for all contacts with the other party. Should there be a change in each Party's contact person, the partner shall inform each other as soon as possible.

Both parties will provide a link on their website to the other's website.

a) ***Official announcement***

An official announcement of the present agreement will be made on both Parties websites as a common statement by the UEMS and the European Society after signature of the agreement. The statement will be also circulated to both Parties constituency.

8. REPRESENTATION

The President of the European Society or an appointed representative of the European Society is invited to take part to the MJC RUD's executive meetings.

Likewise, the President of the UEMS Section and Secretary or another representative of the MJC RUD is invited to take part in meetings of ENETS ADVISORY Board Meetings (the European Society's Executive or an appropriate body).

9. FUNDING

This MoU does not include the exchange of funds between parties.

10. MODIFICATION

This MoU can be modified or amended only by a writing signed by both parties.

11. TERM AND TERMINATION

This MoU is concluded for an indefinite period.

12. EFFECTIVITY

This MoU is effective immediately upon signature of all parties here to.

Appendix 12

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

02/06/2019

Date: _____

UEMS President

European Neuroendocrine Society, Chairman

European Neuroendocrine Society, Treasurer

UEMS Secretary General

UEMS MJC RUD President

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Minutes

Meeting UEMS – ENETS

Participants: Bela Melegh (BM)
Andreas Pascher (AP)
Vassilios Papalois (VP)
Andrea Frilling (AF)

Date: 03 May 2019; 11:30-14:30

Venue: St Mary's Hospital Campus (Paddington), London, UK
Queen Elisabeth Queen Mother (QEQM) Building
Peart Room, #1086 (on the 10th floor of QEQM)

Introduction of participants

Reports

1. VP explains the structure of UEMS with its specialities, sections and competencies. UEMS – ENETS cooperation will be free of any special fee. UEMS is willing to provide administrative advice and help with setting up of examinations.

2. BM presents the areas of activity within the UEMS. He shows an example of a Multidisciplinary Joint Committee which could serve as a template for Neuroendocrine Tumours. Thanks to the support of its Specialist Sections and European Boards, the UEMS contributed significantly to the improvement of post graduate training especially through the development of European Curriculum in each medical specialty as well as the elaboration of Training Standards. Back in 1994, the UEMS adopted its "Charter on Training of Medical Specialists" with an aim to outline the guiding principles for high level Medical Training. European Standards in Medical Training and examples of existing European Training Requirements (ETR), Competence -based training and Assessment for Specialists Sections, Council for European Specialists Medical Assessment (CESMA) including CESMA appraisal will be demonstrated (information available on: https://www.uems.eu/areas-of-expertise/postgraduate-training/european-standards-in-medical-training.

3. AP reports on history, structure, aims and activities of ENETS.

4. AF refers to the letter regarding NET Curriculum sent by ENETS Chairman and ENETS Advisory Board Chairman, respectively to AF and AP on 02/05/2019. They invited AF and AP to create a NET Curriculum task force and present a formal, advanced project outline of the curriculum at the ENETS Advisory Board meeting on 14/11/2019.

Appointment of UEMS- ENETS Committee
VP, BM, AP, and AF uniformly agree to nominate a group of representatives of both societies to coordinate the project. AP and AF will represent ENETS. VP and BM will nominate two UEMS representatives.

Administrative support
UEMS – Ms Marianne Chagon, EU Policy and Coordinator Officer (coordination@uems.eu)
ENETS – TBA

Actions to be taken
-AP and AF, together with the NET Curriculum task force group, to develop a NET ETR. BM and his group to develop NET specific CESMA.
-30 September 2019 - Documents to be exchanged for review.
-14 November 2019 – AP and AF to present the project at ENETS AB Meeting. Possible approval.
-15 January 2020 – submission to UEMS for review
-April 2020 – proposal to be presented at UEMS EC Meeting and possibly approved.

Next meeting
TBA

Drafted by AF
05/05/2020

Appendix 14

UEMS - EUROPEAN UNION OF MEDICAL SPECIALISTS

MULTIDISCIPLINARY JOINT COMMITTEE ON RARE AND UNDIAGNOSED DISEASES

Dr. Joao Grenho
Secretary General of the UEMS
Brussels
Domus Medica

28 January, 2020

Dear Dr Grenho,

Attached please find three separate packages of European Training Requirements (ETR), for which I request inclusion into the agenda points of the next UEMS Council meeting for consideration for approval. As you can see, two of them consist of 3 separate files each, which approach was chosen to generate files with stand-alone documents, that could be used by independent stakeholders involved in the training: while one of them is a single file.

The following documents are attached:

1., The ETR for "Rare and Undiagnosed Diseases", which consist of the next files:
- Training Requirements for the Specialty of Rare and Undiagnosed Diseases
- Description of “Rare and Undiagnosed Diseases” as a Medical Specialty in EU: Aims and objectives for specialist training
- Syllabus for residents and trainees in Rare and Undiagnosed Diseases

2., The European training requirements for the specialty of "Rare Adult Solid Cancers", which consist of the next files:
- Training Requirements for the Specialty of Rare Adult Solid Cancers
- Description of “Rare adult solid cancers” as a Medical Specialty in EU: Aims and objectives for specialist training
- Syllabus for residents and trainees in Rare Adult Solid Cancers

3., European training requirement for "Neuroendocrine Neoplasia Medicine", which is a collaborative effort of the MJC RUD and the European Neuroendocrine Tumor Society (ENETS).

I thank for your kindness, and looking forward to hearig about your decision.

Bela Melegh
MJC RUD president

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Syllabus for residents and trainees in Rare and Undiagnosed Diseases

This a usual syllabus, an outlined summary of major and specific topics to be covered in a training course of a trainee. The goal of the syllabus is to ensure a fair and impartial working material as a connection between the instructor and the trainee. The syllabus is not a road map of the course, nor an organization/direction relaying the instructors' teaching policy to the trainees, so the syllabus is not a learning guide. Instead, the syllabus is a supporting reference material with priorities of training. However, it should be taken as a flexible material. It can differ between training institutions. Since the major pillars of the rare disease ETR rely primarily on internal medicine, neurology, pediatrics and medical genetics, it is strongly recommended to use the UEMS approved ETRs for these specialties as additional training material.

Domain 1: Basics

1.1 Rare disease terms, items, definitions

1.1.1 Rare disease definitions and rare disease basics in medical specialties
1.1.2 Causes of rare diseases
1.1.3 Rare disease clinical research networks
1.1.4 ORPHANET/ORPHACODE
1.1.5 EURODIS (Voice of rare disease patients)
1.1.6 National rare disease policies
1.1.7 International rare disease policies
1.1.8 Living with rare diseases
1.1.9 Rare disease helplines
1.1.10 Specialized social servers
1.1.11 Therapeutic recreational programs
1.1.12 Adapted housing and research centres

Domain 2: Clinical knowledge

2.1 Medical Records in Rare Diseases

2.1.1 Review medical records and identify information sources including databases and literature searches

2.2 Taking a detailed medical and family history and pedigree construction and interpretation

2.2.1 To analyse a clinical history in a relevant, succinct and logical manner
2.2.2 Use interpreters and advocates appropriately
2.2.3 Manages alternative and conflicting views from family, carers, friends and members of the multi-professional team
2.2.4 Assimilates history from the available information from patient and other sources including members of the multi-professional team
2.2.5 Recognises and interprets appropriately the use of nonverbal communication from patients and carers

2.3 Diagnosis, investigation and management of individuals with rare inherited diseases and their families

2.3.1 Examination
- 2.3.1.1 Perform a reliable and appropriate examination to elicit relevant signs of genetic disease
- 2.3.1.2 Perform examination appropriately in situations involving cultural sensitivity
- 2.3.1.3 Understand when additional specialist examination is required
- 2.3.1.4 Recognises the possibility of deliberate harm (both self-harm and harm by others) in vulnerable patients and report to appropriate agencies

2.3.2 Involvement of non-family members in process
- 2.3.2.1 Role of patient advocacy groups
- 2.3.2.2 Role of networks (scientific, patient oriented)

2.3.3 Diagnosis and Management
- 2.3.3.1 Present disease information to a patient in a sensitive and understanding manner
- 2.3.3.2 Use computerized genetic databases and registers for information retrieval
- 2.3.3.3 Present undiagnosed cases to colleagues, including dysmorphology club meetings
- 2.3.3.4 Clearly and openly explain management options
- 2.3.3.5 Record concisely, accurately, confidentially and legibly the appropriate elements of the history, examination, results of investigations, differential diagnosis and management plan

2.3.4 European Reference Networks (ERNs)
- 2.3.4.1 ERNs, structure, function, mission
- 2.3.4.2 CPMS as a diagnostic tool

2.3.5 Decision Making
- 2.3.5.1 Interpret clinical features, their reliability and relevance to clinical scenarios including recognition of the breadth of presentation of common disorders
- 2.3.5.2 Incorporates an understanding of the psychological and social elements of clinical scenarios into decision making
- 2.3.5.3 Construct a concise and applicable problem list using available information
- 2.3.5.4 Construct an appropriate management plan in conjunction with the patient, carers and other members of the clinical team and communicate this effectively to the patient, parents and carers securing their agreement to the course of action
- 2.3.5.5 Define the relevance of an estimated risk of a future event to an individual patient
- 2.3.5.6 Use risk calculators appropriately
- 2.3.5.7 Apply quantitative data of risks and benefits of screening and therapeutic intervention to an individual patient
- 2.3.5.8 Search and comprehend medical literature to guide reasoning
- 2.3.5.9 Generate hypothesis within context of clinical likelihood
- 2.3.5.10 Test, refine and verify hypotheses
- 2.3.5.11 Develop problem list and action plan

2.3.6 Ability to take samples for genetic analysis
- 2.3.6.1 Phlebotomy from adults and children, including those with special needs
- 2.3.6.2 Hair Root Extraction
- 2.3.6.3 Skin biopsy
- 2.3.6.4 Collection of other samples, such as buccal smears, urine samples, etc.

2.3.7 Clinical Photography
- 2.3.7.1 Demonstrate ability to take photographs of sufficient quality for clinical use
- 2.3.7.2 Use of digital photography and storage of data

2.4 Therapeutic aspects and emerging therapies of genetic diseases

2.4.1 Prescribe and oversee enzyme replacement therapies for applicable disorders, including lysosomal storage disorders within a multidisciplinary clinical team consensus

2.4.2 Prescribe other repurposed dugs to specific genetic condition (e.g., losartan) within a multidisciplinary clinical team consensus

2.4.3 Develop a management strategy, including preventative surgery, for men and women with hereditary cancer

2.5 Risk assessment and role in genetic testing

2.5.1 Calculate genetic risk in single gene disorders by hand

2.5.2 Calculate genetic risk by use of a computer programme

2.6 Paediatric genetics including training in Dysmorphology (knowledge of common dysmorphic syndromes, their aetiology and the use of dysmorphology databases) and investigation of learning and intellectual disability in children

2.6.1 Be able to take a relevant history, and perform an appropriate examination, obtain illustrative photographs

2.6.2 Have a rational approach to investigation of children with delayed development and/or dysmorphic syndromes

2.6.3 Formulate differential diagnoses of unknown syndromes. Utilise journals and databases used in syndrome identification

2.6.4 Cultivate critical assessment of database information and case reports to identify uncertainty and subjectivity in syndrome diagnosis

2.6.5 Be able to provide a diagnostic service within a multidisciplinary clinical team

2.6.6 Present and discuss cases with colleagues

2.7 Adult genetics to include knowledge of late onset disorders and disorders with a significant genetic component presenting in adult life (including predictive testing)

2.7.1 Be able to take a relevant history, perform an appropriate examination and formulate clinical diagnoses

2.7.2 Be able to assess patients and families affected by genetic conditions

2.7.3 Judge when it is necessary to sustain supportive relationships with patients with chronic disease

2.7.4 Be able to discuss reproductive options (AID, ICSI, IVF, pre- implantation diagnosis) with the patient and their partner in a sensitive manner

2.7.5 Be able to discuss and formulate integrated care pathways and management plans with individuals/families

2.7.6 Verify diagnoses from old hospital records

2.8 Prenatal Genetics and knowledge about effects of teratogens in foetal development

2.8.1 Interpret family history data

2.8.2 Provide genetic advice and organize testing for women who may undergo preimplantation or prenatal diagnosis

2.8.3 Formulate differential diagnoses and assess prognosis in collaboration with the foetal medicine team

2.8.4 Assess risk to foetus when pregnancies are exposed to hazards such as congenital infections, alcohol, ionising irradiation or drugs

2.8.5 Assess clinical significance of chromosome, DNA and foetal imaging in the context of foetal abnormality

2.8.6 Evaluate foetal post-mortem findings

2.8.7 Interpret the reports of non-invasive prenatal testing (NIPT)

2.9 Genetic screening programmes

2.9.1 Team-working with database managers, genetic associates and nurse specialists in:

2.9.1.1 'Cascade screening' and provision of genetic services for extended families with common single gene disorders (cystic fibrosis, Xp21 muscular dystrophy, fragile X syndrome, Huntington's disease)

2.9.1.2 Family based screening for individuals at high risk of developing cancer

2.9.1.3 Contribute to the maintenance of departmental genetic registry systems

2.9.1.4 Be able to explain the benefits and consequences of screening programmes

2.10 Examination of paediatric and adult patients, knowledge of dysmorphic signs, and main neurologic signs

2.10.1 Physical examination, body measurements and review of medical information

2.11 Gene therapy and its current and future applications

2.11.1 Be able to discuss the pros and cons of gene therapy in relation to a specific disorder and suggest clinical trials, if appropriate

2.12 Common diseases with a genetic component and oligo-/polygenic disorders

2.12.1 Distinguish between classical Mendelian and oligogenic inheritance and be able to calculate the appropriate recurrence risk

2.12.2 Be able to recognize and counsel patients with a strong genetic component

2.13 General knowledge base from UEMS specialities

Allergology
Anaesthesiology
Cardiology
Cardiothoracic Surgery
Connective Tissue Genetics
Dermatology and Venereology
Emergency Medicine
Endocrinology
Gastroenterology
Genetics of Craniofacial Anomalies and Ear Nose and Throat disorders
Genetics of Immunological and Auto-inflammatory Diseases
Geriatrics
Gynaecology and Obstetrics
Haematology
Hepatology
Hereditary metabolic disorders
Infectious Diseases
Internal Medicine
Laboratory Medicine / Medical Biopathology
Malformation, developmental anomalies and rare intellectual disabilities
Medical Genetics
Medical Microbiology
Medical Oncology
Multi-systemic vascular diseases
Nephrology
Neurogenetics
Neurology
Neurosurgery
Occupational Medicine
Oncology
Ophthalmology
Oro-Maxillo-Facial Surgery
Orthopaedics
Traumatology
Otorhinolaryngology
Paediatrics
Pneumology
Prenatal and Reproductive
Pulmonology
Psychiatry
Public Health Medicine
Radiology
Radiation Oncology and Radiotherapy

Rheumatology
Skeletal Disorders
Surgery
Urology/ Urogenital

2.14 List[1] of comprehensive Entrustable Professional Activities (EPAs)

2.14.1 Evaluate and manage a new medical condition in an ambulatory patient and coordinate care between healthcare providers across multiple care settings
2.14.2 Manage the care of patients with rare medical conditions across multiple care settings
2.14.3 Manage the care of patients with complex medical conditions, and/or comorbidities, across multiple care settings
2.14.4 Manage transition of care for adult patients transferring to another care setting
2.14.5 Manage transition of care for young patients transferring from pediatric to adult services
2.14.6 Provide medical consultation to nonmedical specialties
2.14.7 Lead a family meeting to discuss serious news (bad news, end of life care) with a patient and/or family and other health providers
2.14.8 Obtain initial history, perform physical examination, and formulate a management plan for a new ambulatory patient in continuing care
2.14.9 Manage the care of patients with chronic conditions across multiple care settings
2.14.10 Access medical information to provide evidence-based care
2.14.11 Facilitate the understanding of patients, their families, and members of the multidisciplinary team
2.14.12 Recognize and diagnose common nonmedical conditions (i.e., surgical, neurological, dermatologic, etc.) and refer appropriately to other specialty care
2.14.13 Diagnose and comanage patients with complex conditions needing other specialty care (inpatient or outpatient)
2.14.14 Organize and maintain information and knowledge through medical practice to improve personal development when delivering care and educating others (journal club, etc.)
2.14.15 Recognize when palliative care is needed and liaise with palliative care specialists
2.14.16 Counsel patients appropriately
2.14.17 Advocate for individual patients by representing them, supporting them and working for them
2.14.18 Improve patient safety
2.14.19 Provide age appropriate screening and preventative care
2.14.20 Identify and address any need for quality improvement in a clinical setting
2.14.21 Improve the quality and safety of healthcare at both individual and systems levels
2.14.22 Provide telephone management for an ambulatory rare disease patient
2.14.23 Provide care to nonnative speakers in an inpatient or outpatient setting through the use of appropriate translation services
2.14.24 Develop and implement a management plan based on review of outcome data for ambulatory patient population
2.14.25 Provide inpatient and outpatient care for patients with difficulty in accessing appropriate healthcare; advocate for individual patients where needed
2.14.26 Participate in an in-hospital cardiopulmonary resuscitation
2.14.27 Perform common procedures in internal medicine (lumbar puncture, thoracocentesis, central line insertion, joint aspiration)
2.14.28 Undertake a research project (e.g., a degree or diploma, quality improvement, educational opportunity, other)
2.14.29 Develop the practice of lifelong learning
2.14.30 Demonstrate professional behavior at all time

[1] Adopted with revisions from Karen. E. Hauer, Jeffrey Kohlwes, Patricia Cornett, Harry Hollander, Olle ten Cate, Sumant R. Ranji, Krishan Soni, William Iobst, and Patricia O'Sullivan (2013) Identifying Entrustable Professional Activities in Internal Medicine Training. Journal of Graduate Medical Education: March 2013, Vol. 5, No. 1, pp. 54□59 and the Alliance for Academic Internal Medicine. Internal Medicine End of training EPAs, 2012

Domain 3: Detailed and specific Topics

3.1 Detailed Topics

3.1.1 Applied pharmacology
- 3.1.1.1 Drug side effects
- 3.1.1.2 Pharmacovigilance activity
- 3.1.1.3 Pharmacogenomics in drug action
- 3.1.1.4 Pharmacotoxicology
- 3.1.1.5 Side effects, adverse effects

3.1.2 Cancer
- 3.1.2.1 Take a relevant history, perform an appropriate examination and undertake risk estimation using a variety of methods
- 3.1.2.2 Use of cancer registers and other sources to verify diagnoses
- 3.1.2.3 Use disease registers to support follow-up of affected and at-risk patients
- 3.1.2.4 Assessment of screening protocols for at-risk relatives
- 3.1.2.5 Identify at-risk patients and relatives who are eligible to participate in trials of cancer prevention strategies
- 3.1.2.6 Rare cancers; differences and similarities with rare diseases. Types (classification: Pediatric cancers, Hematologic rare neoplasms; Sarcomas; Rare thoracic cancers; Neuroendocrine tumors; Head & neck cancers; Central nervous system tumors; Rare female genital cancers; Rare urological and male genital tumors; Endocrine gland tumors; Digestive rare cancers; Rare skin cancers & non-cutaneous melanoma)

3.1.3 Cardiovascular diseases
- 3.1.3.1 Relevant history, perform an appropriate examination
- 3.1.3.2 Work with bereaved families following sudden adult death
- 3.1.3.3 Rare variants in common polygenic diseases
- 3.1.3.4 Assessment of screening protocols for at-risk relatives
- 3.1.3.5 Coordinate diagnostic and predictive genetic testing in ICC families
- 3.1.3.6 Identify at-risk patients/trios eligible to participate in prevention strategies (e.g., therapeutic trials)

3.1.4 Communicable diseases
- 3.1.4.1 Basics in microbiology
- 3.1.4.2 Rare infectious diseases
- 3.1.4.3 Travellers, migrants and their significance in the spread of communicable diseases
- 3.1.4.4 Diagnostic features

3.1.5 Connective tissue diseases
- 3.1.5.1 Conduct a physical examination appropriate for evaluation of an individual with a suspected connective tissue disorder, including appropriate body measurements (arm span, upper/lower segment ratios, Beighton score, arachnodactyly, hindfoot valgus, pes planus, pectoral abnormalities, etc.)
- 3.1.5.2 Formulate a differential diagnosis for a patient with joint laxity
- 3.1.5.3 Formulate a differential diagnosis for a patient with Marfanoid habitus
- 3.1.5.4 Formulate a differential diagnosis for a patient with aortic dilatation using family history, medical history, and physical examination
- 3.1.5.5 Apply diagnostic criteria to establish a diagnosis of Loeys-Dietz syndrome, including use of imaging (such as evidence of vascular tortuosity)
- 3.1.5.6 Establish the specific type of EDS based on diagnostic criteria
- 3.1.5.7 Apply clinical and laboratory criteria to establish a diagnosis of Stickler syndrome

3.1.6 Craniofacial Anomalies and Ear, Nose and Throat disorders
- 3.1.6.1 Differential diagnosis for craniofacial Anomalies and ear nose and throat disorders
- 3.1.6.2 Differential diagnosis in new-borns identified with congenital deafness either through new-borns screening or clinically

3.1.6.3 Interpret audiologic tests and distinguish different patterns of hearing impairment, including sensorineural and conductive
3.1.6.4 Management plan for a child or an adult with congenital or progressive hearing impairment

3.1.7 Dermatological Diseases
3.1.7.1 Formulate a differential diagnosis for a patient with an ichthyosiform disorder
3.1.7.2 Recognize the features of skin fragility and blistering associated with epidermolysis bullosa
3.1.7.3 Differential diagnosis for a patient with abnormal ectodermal structures (hair, teeth, nails, sweat glands)
3.1.7.4 Differential diagnosis for a patient with premature aging, photosensitivity, vascular lesions or multiple cutaneous neoplasms or hamartomas
3.1.7.5 Order appropriate genetic testing for suspected genodermatoses
3.1.7.6 Cutaneous features that are associated with multisystem disorders

3.1.8 Diseases of malformation, developmental anomalies and rare intellectual disabilities
3.1.8.1 Determine if a congenital anomaly represents a malformation, deformation, disruption, or dysplasia
3.1.8.2 Difference between a syndrome, sequence, and association
3.1.8.3 Congenital anomalies in terms of dysfunction of normal development, both at the level of the embryo and at the level of cellular mechanisms of morphogenesis
3.1.8.4 Explain how foetal exposures/environment can adversely affect foetal growth and/or development
3.1.8.5 Explain how prenatal studies can facilitate diagnostic evaluation
3.1.8.6 Developmental milestones and growth parameters and recognize patterns of abnormal development
3.1.8.7 Differential diagnosis and testing strategy for a patient with one or more major anomalies
3.1.8.8 Specific patterns of dysmorphic features that allow for clinical diagnosis of recognizable genetic conditions
3.1.8.9 Differential diagnosis for a patient with hypotonia and dysmorphic features
3.1.8.10 Differential diagnosis for a patient with disordered growth
3.1.8.11 Differential diagnosis for a patient with autism and dysmorphic features
3.1.8.12 Apply diagnostic criteria to establish diagnosis of congenital anomaly syndromes

3.1.9 Endocrine diseases
3.1.9.1 Formulate a differential for a child with short stature
3.1.9.2 Evaluate a child with ambiguous genitalia, and formulate differential diagnosis
3.1.9.3 Recognize Albright's hereditary osteodystrophy
3.1.9.4 Counsel families with a child with 21-hydroxylase deficiency and adults with infertility, including Klinefelter syndrome, mosaic Turner syndrome, and androgen insensitivity syndrome.
3.1.9.5 Formulate a differential diagnosis for sex reversal
3.1.9.6 Counsel families with multiple endocrine neoplasia (MEN) I or II
3.1.9.7 Evaluate the child with thyroid abnormalities and hearing loss

3.1.10 Gastrointestinal diseases
3.1.10.1 A differential diagnosis for congenital anomalies such as intestinal aganglionosis, pyloric stenosis, intestinal malrotation, etc.
3.1.10.2 A differential diagnosis for patients with hereditary pancreatitis
3.1.10.3 Recognize the need for a cancer control plan for extra intestinal cancers in polyposis syndromes (e.g., breast cancer in Peutz-Jeghers syndrome)

3.1.11 Gynaecological and Obstetric Diseases
3.1.11.1 Stages of embryonic development and their relationship to teratogenic windows in the context of maternal teratogens such as alcohol, medications, or viral exposures
3.1.11.2 Range of normal variation in foetal ultrasound images, the associations of normal variants with and the limitations of ultrasound as a screening modality
3.1.11.3 Counsel and initiate the appropriate prenatal genetic tests when a structural malformation and/or growth abnormality is identified by foetal ultrasound

3.1.12 Hematological diseases
3.1.12.1 Fanconi anemia
3.1.12.2 Genetic causes of familial neutropenia syndromes (e.g., cyclic or severe congenital neutropenia, and

Shwachman-Diamond syndrome), and disorders of neutrophil function (e.g., chronic granulomatous disease)
3.1.12.3 Differential diagnosis for genetic red cell membrane disorders such as hereditary spherocytosis
3.1.12.4 Diagnose and counsel patients with sickle cell trait, beta thalassemia trait, and the various forms of alpha thalassemia trait
3.1.12.5 Plan laboratory assessments for pregnant women with microcytic anemia
3.1.12.6 Counsel families with hemoglobinopathy

3.1.13 Hepatic diseases
3.1.13.1 Differential diagnosis for patients with biliary atresia or arteriohepatic dysplasia
3.1.13.2 Families with hepatic disorders

3.1.14 Immunological and auto-inflammatory diseases
3.1.14.1 A differential diagnosis for a child with severe combined immune deficiency
3.1.14.2 A differential diagnosis for a patient with hypogammaglobulinemia
3.1.14.3 A differential diagnosis for a patient with chronic granulomatous disease
3.1.14.4 Signs of hereditary angioedema
3.1.14.5 Diagnosis for an adult with auto-inflammatory disease

3.1.15 Inherited metabolic diseases
3.1.15.1 Family history data that suggest familial metabolic disease
3.1.15.2 Clinical signs in affected individuals
3.1.15.3 Be able to draw up a differential diagnosis and institute appropriate genetic testing
3.1.15.4 Assessment of symptoms and signs in patients at risk of metabolic disorders
3.1.15.5 Make timely, appropriate referrals to other specialists
3.1.15.6 Identify at-risk patients and relatives who are eligible to therapeutic and preventional strategies

3.1.16 Multi-systemic vascular diseases
3.1.16.1 Formulate a differential diagnosis for multi-systemic vascular diseases

3.1.17 Nephrological diseases
3.1.17.1 Provide genetic counselling for an individual who has or is at risk for infantile or adult polycystic kidney disease
3.1.17.2 Genetic aetiologies that contribute to nephrotic and renal tubular disorders
3.1.17.3 Differential diagnosis between Alport syndrome and other renal disorders
3.1.17.4 Apply diagnostic criteria to establish diagnosis of disorders including Bardet-Biedl syndrome, tuberous sclerosis complex, von Hippel-Lindau syndrome, Meckel syndrome, Zellweger syndrome

3.1.18 Neurodiseases and neuromuscular diseases
3.1.18.1 Recognise family history data that suggest familial neurological disease
3.1.18.2 Clinical signs in affected individuals
3.1.18.3 Differential diagnosis and institute appropriate genetic testing
3.1.18.4 Assessment of symptoms and signs in patients at risk of adult-onset neurogenetic disease
3.1.18.5 Application of protocols for pre-symptomatic diagnosis of Huntington's disease and other neurodegenerative disorders
3.1.18.6 Make timely, appropriate referrals to other specialists such as neurologists, psychologists, psychiatrists, speech therapists

3.1.19 Opthalmological disease
3.1.19.1 Differential diagnosis for a child with microphthalmia/ anophthalmia/ coloboma with or without a congenital anomaly of the central nervous system
3.1.19.2 Ocular from oculocutaneous albinism
3.1.19.3 Diagnostic criteria to establish the diagnosis of various genetic syndromes with supporting ophthalmologic features
3.1.19.4 Clinical trials in gene-replacement treatment strategies for childhood heritable retinal dystrophies

3.1.20 Psychiatric diseases
- 3.1.20.1 Genetic differential diagnosis based on DSM criteria
- 3.1.20.2 Disorders, including Huntington disease, metachromatic leukodystrophy, some forms of porphyria, and Wilson disease may present with psychiatric symptomatology before other symptoms.
- 3.1.20.3 Be able to diagnose, manage and counsel individuals with these disorders
- 3.1.20.4 Inborn errors of metabolism, particularly syndromes elevating ammonia levels, may be associated with altered behaviours that are symptomatic of acute decompensation
- 3.1.20.5 Knowledge of the features, consequences, and guidelines for management of foetal alcohol syndrome and foetal alcohol spectrum disorder (FASD)
- 3.1.20.6 Syndromic aetiologies based on presentation, including sex and age of onset of symptomatology
- 3.1.20.7 Cardinal features and implement management recommendations for microdeletion syndromes associated with behavioural psychopathology as a primary or major component
- 3.1.20.8 Poorly controlled metabolic disorders often have prominent psychiatric consequences

3.1.21 Pulmonary diseases
- 3.1.21.1 Differential diagnosis, for hereditary pulmonary emphysema
- 3.1.21.2 Differential diagnosis, for idiopathic pulmonary hypertension
- 3.1.21.3 Counsel patients with idiopathic pulmonary fibrosis
- 3.1.21.4 Counsel families with or at risk for cystic fibrosis
- 3.1.21.5 Counsel patients with alpha-1-antitrypsin deficiency

3.1.22 Reproductive system
- 3.1.22.1 Preconceptional genetic counselling to couples with sub-/infertility and organize genetic testing
- 3.1.22.2 Preconceptional genetic counselling to couples with genetic and inherited disorders for their reproductive choices including invasive diagnosis, non-invasive testing, and assisted reproductive technologies (ART)
- 3.1.22.3 Different ART options according to the national legislation and European guidelines including preimplantation genetic testing

3.1.23 Skeletal diseases
- 3.1.23.1 Differential diagnosis of a fetus suspected of having a skeletal dysplasia or dysostosis and assess whether the condition is compatible with postnatal survival
- 3.1.23.2 Differential diagnosis for a child with a congenital limb, axial, and/or craniofacial malformation, including teratogenic causes, syndromic causes, and skeletal dysostoses/dysplasias
- 3.1.23.3 Be able to evaluate radiographs and other imaging studies and know when to order further biochemical or molecular genetic tests, as well as which tests are appropriate for a given situation

3.1.24 Teratology
- 3.1.24.1 Historical perspective on teratology
- 3.1.24.2 Mechanisms of teratology
- 3.1.24.3 Epidemiology of congenital malformations
- 3.1.24.4 Types and classes of teratogens
- 3.1.24.5 Effects of teratogens (death, abortion, miscarriage, malformation, etc.)
- 3.1.24.6 Counselling for teratogen exposure
- 3.1.24.7 Genetic inbreeding

3.1.25 Toxicology
- 3.1.25.1 Reproductive toxicology
- 3.1.25.2 Basic toxicological principals
- 3.1.25.3 Organs in detoxification
- 3.1.25.4 Developmental toxicology
- 3.1.25.5 Toxic substances
- 3.1.25.6 Ionising radiation
- 3.1.25.7 Toxicology in society, environmental toxicology, food toxicology, clinical toxicology, risk assessment

3.1.26 Urogenital diseases
- 3.1.26.1 Differential diagnosis for a child with a congenital anomaly of the urogenital tract

Domain 4: Bioinformatics

4.1 Bioinformatics

- 4.1.1 Basic methods of medical statistics
- 4.1.2 Knowledge of the principles of Human Phenotype Ontology
- 4.1.3 Knowledge in the use of large data sets and "big data"
- 4.1.4 Array data analysis and interpretation
- 4.1.5 Next generation sequencing raw data, massive parallel sequencing file types
- 4.1.6 Next generation sequencing data analysis
- 4.1.7 Analysis of WCF files
- 4.1.8 Public sequence domains used for next generation sequence analysis

Domain 5: Rare disease and society

5.1 Rare disease and society

- 5.1.1 Families living with rare diseases
- 5.1.2 Patient advocacy groups
- 5.1.3 Patient advocacy networks (patient perspectives)
- 5.1.4 Medical education in patient families and advocacy groups
- 5.1.5 Awareness on healthcare policy and decision making
- 5.1.6 Specific legislation related to access and coverage for essential medical therapies, role in clinical trials
- 5.1.7 Genetic laws
- 5.1.8 ELSI in rare diseases
- 5.1.9 Rare Disease Day

Domain 6: Logbook Recommendations[2]

6.1 Logbook Recommendation:

- 6.1.1 Purpose: The purpose of the logbook is to document that the applicant has had direct and meaningful involvement in the rare disease evaluation, counseling and management of patients and/or families, and has received appropriate clinical supervision.
- 6.1.2 Requirements: Logbook of the 55 cases must be completed in accordance with the instructions provided in this summary, and anticipates ongoing review of cases between the trainee and their program director, the applicant should assure that all requirements have been fulfilled before submitting the final logbook for review.
- 6.1.3 Case Selection:
  - 6.1.3.1 All cases must be obtained through accredited residency and/or training program.
  - 6.1.3.2 Supervision for case encounters in genetics clinics must be provided by faculty who are certified.
  - 6.1.3.3 All 55 cases must be obtained during the inclusive dates of the applicant's training. No more than 2 cases may be obtained in any one day.
  - 6.1.3.4 Each logbook entry must document a face-to-face interaction between the applicant and an individual patient and/or family. Evaluation, management, or counseling performed via telephone or in group counseling sessions will not be accepted.
  - 6.1.3.5 A given patient or family may appear only once in an applicant's logbook, regardless of the number of encounters with that patient or family.
- 6.1.4 Description of Logbook Headings/Columns:
  - 6.1.4.1 Entry Number: The logbook spreadsheet allows a trainee to enter an unlimited number of cases while in training. For the final logbook that may be requested for audit, you must select 55 cases to submit that fulfill all of the defined requirements. The applicant must be able to identify each case by its entry number if questions arise about a logbook entry
  - 6.1.4.2 Date: The date in month/day/year format identifies when the patient was seen

[2] Based on the American Board of Medical Genetics "Certification in Clinical Genetics and Genomics Logbook Guidelines" http://www.abmgg.org/2019/2019%20Logbook%20Documents/2019%20Clinial%20genetics%20logbook%20FINAL.pdf

6.1.4.3 Patient Age Category: For each case, the patient's age must be defined as Infant (5 cases), Child and Adolescent (20 cases), or Adult (25 cases) or Undiagnosed of any age (5 cases). Age refers to age of the patient on the date of the clinic visit.

6.1.4.4 Diagnosis: **N**o more than 5 cases may have the same specific diagnosis. Variations in genotype or phenotype of a specific diagnosis, such as age of onset or particular mutation, are not considered sufficient to count as separate diagnoses. It is the age at onset and not the age of diagnosis or the age at which the trainee saw the patient that should be taken into account in satisfying this requirement.

For each case, enter the diagnosis using the guidelines below:

6.1.4.4.1 Enter the diagnosis using the OMIM name or an ORPHACODE alternative title. All cases representing the same condition should be entered using the same diagnosis name.

6.1.4.4.2 Do not use abbreviations unless an OMIM/ORPHACODE alternative title.

6.1.4.4.3 Primary diagnosis must be listed first.

6.1.4.4.4 Use the most specific diagnosis for each case when known.

6.1.4.4.5 Log only those cases for which the diagnostic evaluation is complete. For example, "5p deletion syndrome" not "Rule out chromosome anomaly." If making a specific diagnosis was the reason for the referral, for example, is this Marfan syndrome?, use "Marfan syndrome" if the diagnostic evaluation is complete and this is the diagnosis or "Marfan syndrome, excluded" if the diagnostic evaluation is complete and this diagnosis was excluded but a more specific diagnosis could not be made. If a more specific diagnosis could be made, such as Shprintzen-Goldberg syndrome, use the more specific diagnosis.

6.1.4.4.6 If more than one patient or family with the same genetic category, age category, diagnosis, visit date, trainee role(s), and supervisor are recorded, clearly indicate that entries are not duplicated records or members of the same family, as follows: Neurofibromatosis, patient or family 1; Neurofibromatosis, patient or family 2.

6.2 Trainee's Role:

6.2.1 Medical history: involves obtaining pertinent medical information, such as pregnancy history, developmental milestones, and environmental exposures, by patient interview and review of medical records.

6.2.2 Pedigree: includes eliciting information for the construction of a pedigree that includes at a minimum all first and second-degree relatives using standard symbols.

6.2.3 Physical examinations: entails performing a complete physical examination or, if more appropriate, a targeted examination, to assess the system(s) of concern or to look for manifestations of a Mendelian condition in individuals who present for evaluation of a common complex disorder.

6.2.4 Management/Evaluation plan: involves determining recommendations for appropriate tests and/or assessments of medical or psychosocial care for a patient/family.

6.2.5 Testing options/results: includes explaining the technical and medical aspects of diagnostic and screening methods and reproductive options, including associated risks, benefits, and limitations, as well as interpreting and communicating testing results.

6.2.6 Risk assessment: entails performing pedigree analysis and evaluation of medical and laboratory data to determine recurrence/occurrence risks.

6.2.7 Inheritance/risk counseling: involves educating the patient or family about recurrence/occurrence risks and modes of inheritance of the disorder.

6.2.8 Discussion of diagnosis/natural history: includes conveying genetic medical information about the diagnosis, etiology, natural history, prognosis, and treatment/management of the disorder(s) in question.

6.2.9 Psychosocial support/counseling: involves providing short-term, patient or family- centered counseling, psychosocial support, and anticipatory guidance to the family, as well as addressing patient concerns.

6.2.10 Information access: includes literature review and database searches, as well as identification of resources for the patient or family and referring healthcare provider.

6.2.11 Documentation and follow-up: involves writing a consultation report or letter to the family or healthcare provider and recording adequate follow-up notes.

6.2.12 Undiagosed Case: Full description of what happened with the sequence analysis record of deposition of a network (ERN, UDNI, PhenomeCentral, CPMS.

6.3 **Supervisor:** Include the full name, degree(s), and type of certification of the supervisor who was present and was directly responsible for your activities regarding that case

Appendix 14

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Training Requirements for the Specialty of Rare and Undiagnosed Diseases

European Standards of Postgraduate Medical Specialist Training

Preamble

The UEMS is a non-governmental organization representing national associations of medical specialists at the European level. With a current membership of 39 national associations and operating through 43 Specialist Sections and European Boards, the UEMS is committed to promote the free movement of medical specialists across Europe while ensuring the highest level of training that will pave the way to the improvement of quality of care for the benefit of all European citizens. The UEMS areas of expertise notably encompass Continuing Medical Education, Post Graduate Training and Quality Assurance. It is the UEMS' conviction that the quality of medical care and expertise is directly linked to the quality of training provided to the medical professionals. Therefore, the UEMS committed itself to contribute to the improvement of medical training at the European level through the development of European Standards in the different medical disciplines. No matter where doctors are trained, they should have at least the same core competencies.

In 1994, the UEMS adopted its Charter on Post Graduate Training aiming to provide the recommendations at the European level for good medical training. Made up of six chapters, this Charter set the basis for the European approach in the field of Post Graduate Training. With five chapters being common to all specialties, this Charter provided a sixth chapter, known as "Chapter 6", that each Specialist Section was to complete according to the specific needs of their discipline. More than a decade after the introduction of this Chapter, the UEMS Specialist Sections and European Boards have continued working on developing these European Standards in Medical training that reflect modern medical practice and current scientific findings. In doing so, the UEMS Specialist Sections and European Boards did not aim to supersede the National Authorities' competence in defining the content of postgraduate training in their own State, but rather to complement these and ensure that high quality training is provided across Europe.

At the European level, the legal mechanism ensuring the free movement of doctors through the recognition of their qualifications was established back in the 1970s by the European Union. Sectorial Directives were adopted and one Directive addressed specifically the issue of medical training at the European level. However, in 2005, the European Commission proposed to the European Parliament and Council to have a unique legal framework for the recognition of the Professional Qualifications to facilitate and improve the mobility of all workers throughout Europe. This Directive 2005/36/EC established the mechanism of automatic mutual recognition of qualifications for medical doctors according to training requirements within all Member States; this is based on the length of training in the Specialty and the title of qualification. Given the longstanding experience of UEMS Specialist Sections and European Boards on the one hand and the European legal framework enabling Medical Specialists and Trainees to move from one country to another on

the other hand, the UEMS is uniquely positioned to provide specialty-based recommendations. The UEMS values professional competence as "the habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values, and reflection in daily practice for the benefit of the individual and community being served". While professional activity is regulated by national law in EU Member States, it is the UEMS understanding that it has to comply with international treaties and UN declarations on Human Rights as well as the WMA International Code of Medical Ethics.

This document derives from the previous Chapter 6 of the Training Chapter and provides definitions of specialist competencies and procedures as well as how to document and assess them. For the sake of transparency and coherence, it has been renamed as "Training Requirements for the Specialty of Rare and Undiagnosed Diseases". This document aims to provide the basic Training Requirements for each specialty and should be regularly updated by UEMS Specialist Sections, Multidisciplinary Joint Committees, or European Boards to reflect scientific and medical progress. The three-part structure of this document reflects the UEMS approach to have a coherent pragmatic document not only for medical specialists but also for decision-makers at the National and European levels interested in knowing more about medical specialist training.

A "Rare Disorder" (rare disease, orphan disease) is defined according to the European standards as one having a prevalence of not more than five affected persons per 10.000. In different parts of the world, where consanguinity is accepted, different rare diseases can become frequent. Rare diseases can be of genetic origin, multifactorially determined or caused by environmental factors. Rare diseases can be part of different specialities ranging from genetics, through infections to different type of cancers. To date, 5.000-8.000 rare diseases are known, affecting 6-8% of the world population; 80% are of genetic origin while 20% are multifactorial. More than 50% affect children and 30% of them die before the age of 5. The number of rare diseases is increasing partly because of the intense development of genetic testing modalities and the new therapeutic modalities achievable. Rare diseases affect around 30 million EU citizens; they are recognised as a global public helath priority and an exemplar domain for precision public health. A special challenge is the undiagnosed group of rare diseases.

With the formation of the 24 thematic European Reference Networks (ERN) in March 2017, the need for Rare Disease Specialists became evident. ERN's are virtual networks involving healthcare providers across Europe. The aim of ERN's is to harmonize diagnostic strategies and perhaps in the future therapeutic approaches regarding rare diseases across the European Union. The need for rare disease specialists involves all speciality groups and Rare Diseaase Centers from all countries should have a minimum of 10 rare disease specialists. Whereas not all rare diseases are genetic conditions, the genetic departments are expected to feature prominently.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Aims and goals of Rare and Undiagnosed Disease Speciality training and assesment
(Further essential parts of the ETR are described in the supplementary "Description of the specialty" and "Syllabus"):

1. To construct a tool for training and qualification/certification system for service specialists whose goal is to assess, investigate, and diagnose diseases and medical conditions that are rare, having a prevalence of less than 1 in 2.000.
2. To create a system that provides specialist knowledge-based training information about rare and undiagnosed diseases, including recommendations for screening where appropriate.
3. To provide a service that offers education/knowledge base of counselling in relation to reproductive options and prenatal genetics in rare diseases.
4. The primary prevention of rare diseases of multifactorial or nongenetic origin, based on the knowledge and mitigation of risk factors related to medical treatments, maternal health, infections, diet, lifestyles, living environment and workplace
5. The primary and secondary prevention of rare hereditary diseases, according to: i) the choice made by those at risk of having affected offspring, based on full information and expert counselling; ii) effective programmes of newborn screening allowing early measures to prevent the onset of diseases
6. To contribute to the management of patients and families affected by rare diseases, in collaboration with other medical specialists, including treatment.
7. Knowledge on European Reference Networks (ERN), CPMS system essentials.
8. To be advocates, where necessary, for those affected by rare diseases. EURORDIS knowledge base.
9. To conduct and contribute to clinical and genomic research to enhance knowledge of the causation and natural history of rare diseases and conditions.
10. To teach and instruct medical undergraduates and postgraduates in rare and undiagnosed diseases, in order to raise the knowledge base across all medical specialties.
11. To provide a knowledge and skills resource to all medical specialties, including through multidisciplinary meetings.
12. Orphanet and orphacode knowledge base.
13. To provide a service in collaboration with clinical specialists, researchers and geneticists for diagnosis and description of a novel disorder.
14. The European Certificate in Rare and Undiagnosed Diseases is intended to be the main knowledge-based assessment tool for training and assessment across Europe, with the ultimate aim of establishing world class-leading standards in that specialty throughout all countries.
15. The rare cancers are recognised under different specialties (Rare adult solid cancers, pediatric oncology, etc), some basics are still included in this specialty field as well.
16. Special attention and care should be taken for expertise in the undiagnosed fields and disease management. Management of undiagnosed cases, recontacting, data sharing, participation in the existing and emerging networks.
17. Basics of communcable diseases, and selected parts of the rare diseases (including tropical), basics in bacteriology, virology, parasitology. Migration and its communicable diseases consequences.
18. Toxicology, applied pharmacotoxicology, teratology basics.
19. To facilitate connections between individuals affected with the same rare disorder or those with as yet undiagnosed diseases.
20. To contribute to the public awareness for rare diseases.

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

I. TRAINING REQUIREMENTS FOR TRAINEES

1. Content of training and learning outcome

The Rare and Undiagnosed Disease Speciality is a field of medicine concerned with the investigation, diagnosis, treatment, prevention, and research into rare and undiagnosed diseases. The scope of patient care activities includes the recognition of these diseases, the early identification of individuals and families at risk, the identification of the possible underlying (genetic) defect and the preventive care of affected family members and identification of environmental, infectious, toxicological and/or diet/lifestyle-related risk factors to prevent diseases in population.

This specialty training is aimed at giving doctors qualifications in the field of "Rare and Undiagnosed Diseases" to enable them to manage the treatment of patients with rare diseases and their families in light of current and expanding knowledge on the subject, with particular emphasis on understanding the molecular and cellular pathogenic mechanisms of such diseases, and their diagnosis and treatment. Rare disease specialists must also be able to coordinate the follow-up of patients affected by rare diseases.

Elements of knowledge base (see details in Description of Specialty file and in Syllabus)

- *Basic theoretical genetics / Basic science*
- *Clinical/Medical knowledge and specialist-level skills*
- *Genetic counselling and communication skills*
- *Laboratory skills*
- *Maintaining Good Medical Practice*
- *IT skills*
- *Ethics and law*
- *Biobanking and registries*
- *Management training*
- *Teaching*
- *Quality assurance*
- *Research*

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Competencies required to gain by the trainee

- sufficient knowledge and experience to manage a complex rare disease.
- shared knowledge of experts by having several specialists under one roof.
- able to undertake research in the particular rare disease and improve not only the care of one individual, but of other patients with the same condition.
- holistic vision of the patients.
- good communication skills.
- developing patient registries.
- coordinating patient routes and follow-up.

2. Organization of training

a. Schedule of training

The optimal Rare Disease Speciality training is 4 years consisting of 1 year of common trunk and 3 years training in a Rare Disease Center in an accredited program and/or center. The training of 3 years is also accepted, if the candidate has additional year(s) in research related to rare diseases. However, those countries that have a 3 year-course must arrange a preliminary general training, covering medicine and pediatrics if possible, before, and separate from, the 4 year specialist training. The specialist training is definied here as training in institutions involved in rare disease care. This includes training in the units with profiles of following medical specialties with rare disease outpatient clinic and/or ward: Allergology, Anaesthesiology, Cardiology, Cardiothoracic Surgery, Dermatology and Venereology, Emergency Medicine, Endocrinology, Gastroenterology, Geriatrics, Gynaecology and Obstetrics, Infectious Diseases, Internal Medicine, Laboratory Medicine / Medical Biopathology, Medical Genetics, Medical Microbiology, Medical Oncology, Nephrology, Neurology, Neurosurgery, Occupational Medicine, Ophthalmology, Oro-Maxillo-Facial Surgery, Orthopaedics, Traumatology, Otorhinolaryngology, Paediatrics, Pneumology, Psychiatry, Public Health Medicine, Radiology, Radiation Oncology and Radiotherapy, Rheumatology, Surgery, Urology. The key purpose of this is the acquisition of core clinical skills. Depending on national regulations, the training may start immediately after completion of medical school or as a sub-speciality qualification of 2 years built on Clinical/Medical/Human Genetics speciality. Trainees must maintain an accurate logbook of their training and rotations.

Optimal training would be:
- 1 years common medical trunk training including some of the following: general practice, pediatrics (including pediatrics neurology ward), internal medicine, emergency unit, and genetics.
- 3 years different specialty oriented practice including the previously mentioned specialities.

b. Curriculum of training

The general aim of the training program is to enable the Rare Disease Specialist to work effectively as a consultant. The trainee must demonstrate the ability to record and convey patient details of history, examination and investigation to senior staff. The trainee must communicate effectively with patients and relatives, and be able to pass on both technical information in a way that it can be received with understanding, and distressing information in a sensitive and caring manner.

c. Assessment and evaluation

The European Certificate in Rare and Undiagnosed Diseases (ECRUD) is intended to be the main knowledge-based assessment tool for training and assessment across Europe and ultimately for the entire continent's experts, with the aim of establishing world class-leading standards in that specialty throughout all countries.

Countries will use assessment strategies appropriate to their needs, provided that they introduce their own training and assessment systems. In due course there will be a move to a common approach to determining whether an individual is suitable to be recognized as a 'European medical specialist with additional rare and undiagnosed diseases competence'. Thus, there will need to be an assessment of knowledge, through a form of written examination. This examination would use scenarios from an agreed list of core clinical conditions and test knowledge in the areas of relevant science and clinical practice (diagnosis, investigation, interpretation, prevention and treatment). This assessment may take the form a 'best of five' (multiple choice) format, but has yet to be decided. Oral exam can be part of the process as well.

Continuous medical education (CME) and continuous professional development (CPD) to keep updated with developments in diagnosis and management of rare conditions as well as of global professional skills is an obligation of the accredited expert. Type, duration, content and monitoring of CME/CPD activity need to be established and will fall under the authority of boards that should consider the general recommendations of the UEMS. The UEMS provides European Accreditation of CME (EACCME) for international events according to defined quality standards. It is recommended that trainees in the rare disease field are introduced to CME/CPD during their postgraduate training period.

The ECRUD examination will be a joint development of the UEMS Multidisciplinary Joint Committee (UEMS-MJC RUD) and the sections, MJC-s, National Medical Associations, and of the European scientific societies, world networks, like the Undiagnosed Disease Network International (UDNI) intended to join in this effort. The examination is overseen and supervised by the Examination Steering Committee. It will be open to candidates who are trainees or fully trained experts from any nation. The ECRUD will definitely bean excellence exam, and will be valid for practice only in countries where it is ratified as an official certificate for this purpose by national regulatory bodies or organisations.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

II. TRAINING REQUIREMENTS FOR TRAINERS

1. Process for recognition as trainer

a. Requested qualification and experience

Trainers/examiners should be certified rare disease specialists and must be recognized by a European or national authority. Trainers should provide evidence of academic activities (clinical and/or basic research, publications in peer reviewed journals and participations in clinical genetic scientific meetings) and professional experience. They should possess the necessary administrative, communicative, teaching and clinical skills and commitment to conduct the program. Trainers and Training Program Directors must be in active clinical practice and engaged in training in the training center. Training Program Director must be a certified specialist for a minimum of 5 years. They organize the activities of the educational program in all institutions that participate in the program.

b. Core competencies for trainers

1. Familiar with major and influential aspects of rare diseases.
2. Experienced in teaching and in supporting learners.
3. Trained in the principles and practice of medical education.
4. Act as a lecturer to a peer-audience on a regular basis, attend national meetings and be able to demonstrate appropriate participation in continuing professional development.
5. Able to recognize trainers whose professional behavior is unsatisfactory and initiate corrective and supportive measures as needed.

2. Quality management for trainers

Trainers and Program Directors will have their job description agreed with their employer, which will allow them sufficient time for support of trainees. Feedback from trainees is necessary for optimal training. The educational work of trainers and Program Directors will be appraised no less than an annual basis within their Institution as local circumstances determine.

III. TRAINING REQUIREMENTS FOR TRAINING INSTITUTIONS

1. Process for recognition as training center

a. Requirements for staff and clinical activities

A training center is a place, or number of places, where trainees are able to develop/acquire their competencies in rare diseases. Thus, training may take place in a single institution, or in a network of institutions working together, to provide training in the full spectrum of clinical conditions and skills detailed in the curriculum. A training institution must have national accreditation, in

agreement with UEMS standards, and should possess an adequate infrastructure and offer qualitative and quantitative clinical exposure.

Each participating institution in a network must be individually recognized as a provider of a defined section of the curriculum. Training centers must have a sufficient throughput of patients, an appropriate case-mix to meet training objectives, and be adequately resourced with teaching staff. The training must expose the trainee to a broad range of clinical experience.

The training of a trainee will be led and managed by a specialist. This specialist will be active in the practice, with personal responsibility for the management of patients with a wide range of rare diseases. Within a training center there should be a team of specialists, each with subspecialty expertise and able to supervise and train a trainee. Allied specialties must be present to a sufficient extent to provide the trainee with the opportunity to develop his/her skills in a multidisciplinary approach to patient care. There is no specific trainee/trainer ratio required, but there should be a minimum of two teachers in a training center, and it is likely that non-medical healthcare professionals will also be engaged.

The trainee should be involved in the diagnosis and management process of new patients (out-patients and in-patients), as well as their follow up. A trainee must demonstrate increasing personal responsibility for the global care of patients with rare disorders. There should be written general guidelines within the training institution concerning patient care and patient information (including informed consent), referrals, medical records, documentation, on-call and back-up schedules, attendance at conferences and educational/training courses.

The staff of a training center should engage collaboratively in regular reviews and audit of the center's clinical activity and performance. There should be regular multi-disciplinary meetings to determine optimal care for patients, involving both medical and other healthcare professionals. There will be clinical engagement beyond the Center with other clinical groups such as Rehabilitation Medicine, Orthopedics, Pediatrics, Surgery, Obstetrics and Gynecology, Dermatology, Ophthalmology, etc.

Specialist staff appointed to a training center will have completed all training requirements themselves and will have been trained also in teaching and mentoring trainee staff, and working in a multidisciplinary team with lab and genetic counsellors.

b. Requirements for equipment, accommodation

A training center should have sufficient equipment and support to enable the clinical practice that would be expected of a training center and thus provide the necessary educational opportunities for trainees.

The trainee must have adequate time and opportunities for practical and theoretical study and have access to adequate professional literature.

Computing and Information Technology and library resources must be available. All trainees must engage in clinical audits and have the opportunity to engage in research.

2. Quality Management within Training Institutions

Participation of the training institution in a certified quality management program with an external auditing process on a regular basis is consistent with good governance. Criteria of quality management at specialty training institutions include the following:

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Accreditation

Training institutions need to be accredited with competent National Medical Boards. Additional accreditation on a supra-national level, such as that provided by an European body, is strongly recommended.

A training institution must have an internal system of medical audit or quality assurance. Quality assurance must be an integral part of the training program of all training institutions/networks. A national registry of approved institutions/networks should be available.

Internal regulations: There should be written general guidelines within the training institution concerning patient care and patient information (including informed consent), referrals, medical records, documentation, leave (annual, study), maternity/paternity, residents' working schedules, attendance at conferences and educational activities. These should be available to staff and trainees.

Clinical governance

Employee structure at training institutions needs to be designed in a way to accommodate for specialty training. Workload has to be managed with a priority on training.

Manpower planning

Training institutions should appoint a coordinator responsible for the composition, implementation and supervision of a specialty training program. Roles of trainer and trainee need to be clearly defined. Allotted time of at least one day per workweek should be implemented for specialty training interaction.

Manpower planning is under the jurisdiction of each member state according to their needs for rare disease specialists.

Regular report

Annual reports on various aspects of an institution's specialty training program should be made publicly available.

External audit

Training institutions should appoint a coordinator who is also responsible for compliance of the training program with current guidelines, directives or regulations of competent medical boards, as well as the local medical school.

Transparency of training programs

Based on national and regional guidelines, UEMS strongly encourages training institutions to formulate defined training programs and make them publicly available (e.g., on their website). It is

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

expected that a training center would publish details of the training provision available with details of the clinical service it provides and the trainers. Such information would include the training programs, the nature of the clinical or laboratory experiences in which a trainee would be engaged, and the support and interaction with the trainer and Program Director. There would be a named individual whom a prospective trainee might contact to discuss the program.

Feedback from trainers and trainees

Feedback about program quality from both trainers and trainees must be systematically sought, analyzed and acted upon. Trainers and trainees should be actively involved in using its results for program improvement and development.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS 2020/xxx

Description of "Rare and Undiagnosed Diseases" as a Medical Specialty in EU: Aims and objectives for specialist training

Specialty Profile

Care of rare and undiagnosed disease patients is a multidisciplinary medical specialty concerned with the provision of medical services to individuals, families and groups of affected individuals who have, or are at risk of having, conditions that are differentiated from common diseases primarily by their low incidence or prevalence. Such care includes diagnostic and counselling services that provide information about each condition and its implications, including management, prognosis, screening, prevention and reproductive options, as well as therapeutic possibilities. Information provided is based on clinical assessment, individual or family medical information, conventional laboratory investigations, imaging, and specialized genetic tests that can require complex interpretation. Besides conventional laboratory genetics (cytogenetics, molecular genetics, biochemical genetics), novel components of the services include specialized genetic and genomic approaches such as next generation sequencing and array technologies. The genetic studies include integrated clinical and laboratory services in rare disease management involving any disorder with a significant genetic component, whether inherited or sporadic.

Dedicated institutions already exist in several EU recognized medical specialties, with full medical career training systems. However, while there may be institutions or units that specialize in one or a few types of rare disease, institutions devoted exclusively to rare and undiagnosed diseases are scarce or lacking. As internal medicine, neurology, medical genetics and paediatric units often receive rare disease cases, these units could be re-organized into spokes of hub-and-spoke networks for rare diseases, which could improve care and provide career training specifically focused on rare diseases. Such full-range training is lacking at the moment. The existing educational pathways should be modified to provide education on rare diseases with a multidisciplinary perspective. They should be

flexible enough to accommodate educational needs that cover a spectrum of knowledge bases, including those that address all rare diseases and those that target only a limited number of rare conditions. These educational pathways could be provided in collaboration with the ERNs, and by the European university system. They should include courses on rare diseases, based on a broadly agreed-upon syllabus, and clinical fellowships on selected rare diseases. There should be an examination, with a certification of competence. All this could give rise to an integrated system that will produce experts on rare and undiagnosed diseases, who will ultimately become professionals with dedicated careers at the centres of hub-and-spoke networks. Due to the differences in European health care systems across member states, there may be different national emphases on the various elements of this training programme. We propose below a set of minimum criteria that will be recognized in programmes throughout the EU but recognize that different countries may extend these in different ways.

This document relates to medically qualified individuals intending to acquire UEMS CESMA certification and training in the specialty of rare diseases. It recognizes that there may be areas of overlap with training programmes for other genetic professionals, especially in internal medicine, paediatrics, medical genetics, and neurology and that there may be opportunities for joint training for periods of the course.

One challenge for medical education in rare diseases, which differentiates it from common diseases (including genetic diseases), is that the rare disease discipline lacks reinforcement of recently acquired information due to the small patient numbers. When a physician attends an educational event on a common disease, there will likely be encounters with patients having that disease soon and often. The same does not apply when a disease is rare. The framework of any educational initiative in rare diseases must take into account this challenge.

Entry criteria

These may vary from country to country but would generally include a specified period of general medical training that includes an adult +/- paediatric +/- prenatal medicine “internship”, prior to entering specialty training in rare disease units. Some countries may have a minimum period of training to be undertaken before specialisation. Essentially, the duration of the training is 4 years, with a year of common trunk.

Educational goals

A concise description is provided below, with more details available in the Syllabus. This knowledge base lists the hallmarks of a trained medical doctor ready for qualification for the umbrella exam (certification) in rare diseases.

Knowledge and Skills

Basic theory and fundamentals of rare disease genetics

- Cellular and molecular mechanisms that underpin human inheritance
- Chromosome structure and function, mitosis and meiosis, and the origin of aneuploidy and other imbalances
- The structure of DNA and RNA, replication, transcription and translation.
- Genetic epidemiology and biostatistics
- Risk assessment
- Population genetics, the principles of screening, and basic mathematical genetics
- Bioinformatics and basics of sequencing technology/testing
- Epigenetics
- Pharmacogenetics / pharmacogenomics
- Principles of acquired genetic disorders

Clinical knowledge and skills

- Common and unusual patterns of inheritance
- Taking a detailed medical and family history, pedigree construction
- Ability to perform genetic risk assessment, including the use of Bayes' Theorem to incorporate conditional risk information
- Ability to undertake risk assessment
- Diagnosis, investigation and management of individuals and their families with rare inherited/genetic diseases
- Therapeutic aspects and emerging innovative therapies in rare diseases
- Paediatric genetics including training in dysmorphology (knowledge of common dysmorphic syndromes, their aetiology and the use of dysmorphology databases)
- Adult rare disorders, including knowledge of late onset diseases and conditions with a significant genetic component presenting in adult life
- Prenatal rare diseases paradigms, fetal dysmorphology, and knowledge of the effects of common teratogens on fetal development
- Screening programmes
- Competent clinical examination of both paediatric and adult patients, especially in relation to dysmorphic signs and features, and neurological examination and interpretation
- Gene therapy, its current and future applications, and other strategies for the treatment of genetic disease.

- Common diseases with a rare component/variant
- Multifactorial/polygenic disorders in rare disease fields
- Sub-specialty areas, including:
    - Inherited metabolic disorders
    - Neurogenetic diseases
    - Neuromuscular rare diseases
    - Cardiovascular genetics
    - Reproductive genetics
    - Other subspecialties of specific interest to the trainee, e.g., connective tissue disorders, immunology, etc.

Genetic counselling and communication skills

- Training in genetic counselling for all types of genetic diseases and genetics-related situations encountered in practice. This includes pre- and post-testing counselling in relation to reproductive options, including predictive genetic testing. Where applicable, training in co-counselling with other professionals, with specialists in other fields of medicine
- Understanding and handling of emotional reactions and personal and family crises in relation to the impact of genetic disease and the genetic diagnostic process
- Understanding ethical, legal and social issues, and the importance of consent and confidentiality
- Development of good communication skills with patients and families, colleagues in medical care centres and other specialists and healthcare professionals

Laboratory skills

- Thorough knowledge of principles of classic laboratory techniques used in genetic diagnostic testing
- Thorough knowledge of new laboratory techniques used in genetic diagnostic testing, including SNP and CGH arrays, whole genome sequencing and exome sequencing
- Understanding the interpretation of results from cytogenetic, molecular genetic, biochemical genetic and genomic analyses (array, exome and whole genome analyses)
- Knowledge about preanalytical handling of samples and logistics
- Awareness of quality issues in genetic testing
- Knowledge of international nomenclature systems used in genetic reporting
- The time spent and the practical expertise gained in laboratory work may vary among countries, but it should be sufficient to ensure highly specialized knowledge.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Other aspects of the Training Programme

Maintaining good medical practice

- Understand and practice medical professionalism, honesty, integrity, an aspiration to excellence, fairness, and avoidance of discrimination
- Develop a commitment to lifelong learning through continuing professional development and attend relevant courses and conferences.
- Participate in audit and clinical governance
- Adhere to accepted consent and confidentiality procedures
- Timely management of medical documentation and communication with patients, families, and professionals

Biobanking

- Understand principles of biobanking
- Awareness of ELSI issues

IT skills

- Use of information technology including online resources and databases related to human genetics
- Rare diseases codification and ontologies
- Awareness and use of online data sharing resources

Ethics and law

- Understand ethical, legal and social issues in relation to genetic and genomic medicine
- Issues relating to patient confidentiality, consent and disclosure of results.

Management training

- Knowledge of national laws relating to genetic services and practice, general healthcare policy, goals and priorities
- Understanding the organization and management of genetic services
- Opportunities to participate in departmental/service activities related to organizational planning, financial management, and monitoring and maintaining quality standards
- Development of multidisciplinary team operations and leadership skills

Teaching

- Develop teaching skills by participating in the education and training of various categories of staff
- Involvement with patient groups and patient/family education

Supplementary education and training

- Subspecialty training: Some trainees will elect to develop expertise in a subspecialty area such as cancer genetics, dysmorphology, neurogenetics, etc. This may also vary from country to country.
- Knowledge and understanding of the principles of evidence-based medicine
- Involvement and initiatives in courses, programmes and social issues related to rare diseases
- Knowledge of patient registries, patient support organisations

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Technicals

- A written agreed curriculum for the training period should be set up as a contract between the trainee and the supervisor if not otherwise determined by national regulations
- Trainees should maintain a Training Logbook including details of clinical and laboratory experience, all educational activities, research, and publications
- A mechanism should be in place for continuous assessment of trainees against agreed quality standards; some countries will have a nationally prescribed system for assessment and certification
- Specialist examination may be compulsory in some countries

Research

- Medical genomics has a rapidly changing knowledge base and during specialty training participation in research should be encouraged. Some trainees may wish to participate in scientific projects and research leading to a higher academic degree. On completion of training, some academic clinical/medical geneticists will continue to lead research programmes whilst many others will collaborate with laboratory-based colleagues within a broader team.
- Understand the principles of research methodology including clinical trials

Time frame for specialist training

- The training period should involve a minimum of 4 years full time work, with the option of one additional year spent in another specialty before, after, or as a part of the specialist training. Part time work would extend the training period.
- An educational training programme will be agreed for each trainee according to a specialty-specific curriculum.
- In the longer training period (5 years), up to one year could be in another speciality relevant to rare diseases.
- The time spent in laboratory work may vary among countries according to national curricula.
- A period of research resulting in a PhD/other higher exam may, if appropriate, replace training for a variable period of time according to national guidelines. However, in absence of national guidelines, it is recommended that this time period should not be longer than 1/3 of the total training period.

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Syllabus for residents and trainees in Rare Adult Solid Cancers

The basic goal of this syllabus is to provide an understanding between the instructor and trainee so there is minimal confusion in the topics, with clear expectations. It is not a classical syllabus as it contains descriptions from different areas, but it still summarizes major and specific topics that should be covered during the training course of a resident. This syllabus is intended as supporting reference material, and the precise content and priorities of training may vary in different training institutions. The syllabus can also be modified to reflect each instructor's teaching philosophy towards the trainees.

1. There are scientific publications, web pages, and conference materials available online that could be used for educational purposes for various types of rare adult solid cancers. This is a comprehensive summary of them.

2. There are significant differences in the number of available scientific publications and reviews for different rare adult solid cancers. Some, like sarcomas, have a very robust literature, while others have been sparsely researched and consequently the availability of study materials is quite poor.

3. These differences also apply to life events and natural history. In the list of the EU CE accredited events there is a strong underrepresentation for some types of rare adult solid cancers.

4. Some conferences in this area have a long history, and the thought leaders in the specific fields are involved. In such cases the agendas of the conferences are designed to provide excellent education about best clinical practices for these rare adult solid cancers, opportunities to share major advances in research, and sessions that support the development of new collaborations and new investigators. For other cancers established conferences with solid reputations do not yet exist.

5. These imbalances will persist unless policy makers and research funders provide more attention for research, treatment, and networking on underrepresented rare tumour types. They may also be addressed by the ERNs, or by the UEMS, as recognised stakeholders in improving medical education.

6. As well, there are barriers in the communication of JARC proposals to the ERNs. All ERNs that are involved in rare cancer have made very impressive progress in all fields, including

education. However, communication among ERNs about their education efforts is sparse and not officially regulated. Therefore, we will not have in the near future mutual and harmonised indicators for successful knowledge implementation, which will hinder efforts at assessment.

Domain 1.: Fields of rare adult solid cancers/literature

1.1. Head and neck cancers

1.1.1. Epithelial tumours of nasal cavity and sinuses

Qin Y, Lu Y, Zheng L, Liu H. Ghost cell odontogenic carcinoma with suspected cholesterol granuloma of the maxillary sinus in a patient treated with combined modality therapy: A case report and the review of literature. Medicine. 2018;97(7):e9816. Epub 2018/02/15. doi: https://doi.org/10.1097/md.0000000000009816. PubMed PMID: 29443742; PubMed Central PMCID: PMCPmc5839843.

Takakura H, Tachino H, Fujisaka M, Nakajima T, Yamagishi K, Ishida M, et al. Lymphoepithelial carcinoma of the maxillary sinus: A case report and review of the literature. Medicine. 2018;97(28):e11371. Epub 2018/07/12. doi: https://doi.org/10.1097/md.0000000000011371. PubMed PMID: 29995775; PubMed Central PMCID: PMCPmc6076030.

Thompson LDR, Franchi A. New tumor entities in the 4th edition of the World Health Organization classification of head and neck tumors: Nasal cavity, paranasal sinuses and skull base. Virchows Archiv : an international journal of pathology. 2018;472(3):315-30. Epub 2017/04/27. doi: https://doi.org/10.1007/s00428-017-2116-0. PubMed PMID: 28444451.

Zhang N, Zhou B, Huang Q, Chen X, Cui S, Huang Z, et al. Multiple metastases of clear-cell renal cell carcinoma to different region of the nasal cavity and paranasal sinus 3 times successively: A case report and literature review. Medicine. 2018;97(14):e0286. Epub 2018/04/06. doi: https://doi.org/10.1097/md.0000000000010286. PubMed PMID: 29620646; PubMed Central PMCID: PMCPmc5902287.

Zhenwei C, Zhaoming W, Hongqi S, Qinwei L. Renal cell -like carcinoma of the nasal cavity: a case report and review of the literature. Diagnostic pathology. 2017;12(1):75. Epub 2017/10/19. doi: https://doi.org/10.1186/s13000-017-0660-1. PubMed PMID: 29041930; PubMed Central PMCID: PMCPmc5645912.

1.1.1.1. Squamous cell carcinoma with variants of nasal cavity and sinuses

1.1.1.2. Lymphoepithelial carcinoma of nasal cavity and sinuses

1.1.1.3. Undifferentiated carcinoma of nasal cavity and sinuses

1.1.1.4. Intestinal type adenocarcinoma of nasal cavity and sinuses

1.1.2. Epithelial tumours of nasopharynx

Outh-Gauer S, Alt M, Le Tourneau C, Augustin J, Broudin C, Gasne C, et al. Immunotherapy in head and neck cancers: A new challenge for immunologists, pathologists and clinicians. Cancer treatment reviews. 2018;65:54-64. Epub 2018/03/17. doi: https://doi.org/10.1016/j.ctrv.2018.02.008. PubMed PMID: 29547766.

Shanti RM, O'Malley BW, Jr. Surgical Management of Oral Cancer. Dental clinics of North America. 2018;62(1):77-86. Epub 2017/11/12. doi: https://doi.org/10.1016/j.cden.2017.08.005. PubMed PMID: 29126495.

Takakura H, Tachino H, Fujisaka M, Nakajima T, Yamagishi K, Ishida M, et al. Lymphoepithelial carcinoma of the maxillary sinus: A case report and review of the literature. Medicine. 2018;97(28):e11371. Epub

2018/07/12. doi: https://doi.org/10.1097/md.0000000000011371. PubMed PMID: 29995775; PubMed Central PMCID: PMCPmc6076030.

Zhang WL, Ma S, Havrilla L, Cai L, Yu CQ, Shen S, et al. Primary thyroid-like low-grade nasopharyngeal papillary adenocarcinoma: A case report and literature review. Medicine. 2017;96(47):e8851. Epub 2018/02/01. doi: https://doi.org/10.1097/md.0000000000008851. PubMed PMID: 29381996; PubMed Central PMCID: PMCPmc5708995.

Sun Q, Chen M, Sun Y, Chen X, Xu H, Rong L, et al. Cervical metastasis of gingival carcinoma misdiagnosed as branchiogenic carcinoma, a rare entity - report of a case and review of literature. BMC oral health. 2017;17(1):139. Epub 2017/12/01. doi: https://doi.org/10.1186/s12903-017-0435-9. PubMed PMID: 29183323; PubMed Central PMCID: PMCPmc5706288.

1.1.2.1. Squamous cell carcinoma with variants of nasopharynx

1.1.2.2. Papillary adenocarcinoma of nasopharynx

1.1.3. Epithelial tumours of major salivary glands and salivary-gland type tumours

Li Q, Huang P, Zheng C, Wang J, Ge M. Prognostic significance of p53 immunohistochemical expression in adenoid cystic carcinoma of the salivary glands: a meta-analysis. Oncotarget. 2017;8(17):29458-73. Epub 2017/02/17. doi: https://doi.org/10.18632/oncotarget.15297. PubMed PMID: 28206977; PubMed Central PMCID: PMCPmc5438744.

Lopez F, Williams MD, Skalova A, Hellquist H, Suarez C, Nixon IJ, et al. How Phenotype Guides Management of the Most Common Malignant Salivary Neoplasms of the Larynx? Advances in therapy. 2017;34(4):813-25. Epub 2017/02/23. doi: https://doi.org/10.1007/s12325-017-0494-y. PubMed PMID: 28224460.

Ord RA, Ghazali N. Margin Analysis: Malignant Salivary Gland Neoplasms of the Head and Neck. Oral and maxillofacial surgery clinics of North America. 2017;29(3):315-24. Epub 2017/05/30. doi: https://doi.org/10.1016/j.coms.2017.03.008. PubMed PMID: 28551337.

Falk N, Weissferdt A, Kalhor N, Moran CA. Primary Pulmonary Salivary Gland-type Tumors: A Review and Update. Advances in anatomic pathology. 2016;23(1):13-23. Epub 2015/12/10. doi: https://doi.org/10.1097/pap.0000000000000099. PubMed PMID: 26645458.

Cuthbertson DW, Raol N, Hicks J, Green L, Parke R. Minor salivary gland basal cell adenocarcinoma: a systematic review and report of a new case. JAMA otolaryngology—head & neck surgery. 2015;141(3):276-83. Epub 2015/01/03. doi: https://doi.org/10.1001/jamaoto.2014.3344. PubMed PMID: 25555241.

1.1.3.1. Epithelial tumours of major salivary glands

1.1.3.2. Salivary gland type tumours of head and neck

1.1.4. Epithelial tumours of hypopharynx and larynx

Caroppo D, Salerno G, Merolla F, Mesolella M, Ilardi G, Pagliuca F, et al. Coexistent Squamous Cell Carcinoma and Granular Cell Tumor of Head and Neck Region: Report of Two Very Rare Cases and Review of the Literature. International journal of surgical pathology. 2018;26(1):47-51. Epub 2017/08/09. doi: https://doi.org/10.1177/1066896917724513. PubMed PMID: 28783989.

Zhang Q, Xu H, You Y, Zhang J, Chen R. High Gpx1 expression predicts poor survival in laryngeal squamous cell carcinoma. Auris, nasus, larynx. 2018;45(1):13-9. Epub 2017/06/24. doi: https://doi.org/10.1016/j.anl.2017.05.012. PubMed PMID: 28641905.

Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. CA: a cancer journal for clinicians. 2017;67(1):31-50. Epub 2016/11/30. doi: https://doi.org/10.3322/caac.21386. PubMed PMID: 27898173.

Winquist E, Agbassi C, Meyers BM, Yoo J, Chan KKW. Systemic therapy in the curative treatment of head and neck squamous cell cancer: a systematic review. Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale. 2017;46(1):29. Epub 2017/04/06. doi: https://doi.org/10.1186/s40463-017-0199-x. PubMed PMID: 28376866; PubMed Central PMCID: PMCPmc5381126.

Wollenberg B. Cancer Immunology and HPV. Recent results in cancer research Fortschritte der Krebsforschung Progres dans les recherches sur le cancer. 2017;206:243-8. Epub 2016/10/05. doi: https://doi.org/10.1007/978-3-319-43580-0_19. PubMed PMID: 27699544.

1.1.4.1. Squamous cell carcinoma with variants of hypopharynx

1.1.4.2. Squamous cell carcinoma with variants of larynx

1.1.5. Epithelial tumours of oropharynx

Panwar A, Interval E, Lydiatt WM. Emergence of a Novel Staging System for Oropharyngeal Squamous Cell Carcinoma Based on HPV Status. Oncology (Williston Park, NY). 2017;31(12):e33-e40. Epub 2018/01/04. PubMed PMID: 29297174.

Gross ND, Hanna EY. The Role of Surgery in the Management of Recurrent Oropharyngeal Cancer. Recent results in cancer research Fortschritte der Krebsforschung Progres dans les recherches sur le cancer. 2017;206:197-205. Epub 2016/10/05. doi: https://doi.org/10.1007/978-3-319-43580-0_15. PubMed PMID: 27699540.

Hussein AA, Helder MN, de Visscher JG, Leemans CR, Braakhuis BJ, de Vet HCW, et al. Global incidence of oral and oropharynx cancer in patients younger than 45 years versus older patients: A systematic review. European journal of cancer (Oxford, England : 1990). 2017;82:115-27. Epub 2017/06/28. doi: https://doi.org/10.1016/j.ejca.2017.05.026. PubMed PMID: 28654785.

Nakano T, Motoshita J, Tanaka R, Okabe M, Tamae A, Shiratsuchi H, et al. Primary combined small cell carcinoma and squamous cell carcinoma of the oropharynx with special reference to EGFR status of small cell carcinoma component: Case report and review of the literature. Auris, nasus, larynx. 2017;44(4):472-8. Epub 2016/08/09. doi: https://doi.org/10.1016/j.anl.2016.07.011. PubMed PMID: 27496009.

Shanti RM, O'Malley BW, Jr. Surgical Management of Oral Cancer. Dental clinics of North America. 2018;62(1):77-86. Epub 2017/11/12. doi: https://doi.org/10.1016/j.cden.2017.08.005. PubMed PMID: 29126495.

1.1.5.1. Squamous cell carcinoma with variants of oropharynx

1.1.6. Epithelial tumours of oral cavity and lip

Madera Anaya MV, Franco JV, Merchan-Galvis AM, Gallardo CR, Bonfill Cosp X. Quality assessment of clinical practice guidelines on treatments for oral cancer. Cancer treatment reviews. 2018;65:47-53. Epub 2018/03/17. doi: https://doi.org/10.1016/j.ctrv.2018.03.001. PubMed PMID: 29547765.

Shapiro M, Salama A. Margin Analysis: Squamous Cell Carcinoma of the Oral Cavity. Oral and maxillofacial surgery clinics of North America. 2017;29(3):259-67. Epub 2017/07/16. doi: https://doi.org/10.1016/j.coms.2017.03.003. PubMed PMID: 28709529.

Lin A. Radiation Therapy for Oral Cavity and Oropharyngeal Cancers. Dental clinics of North America. 2018;62(1):99-109. Epub 2017/11/12. doi: https://doi.org/10.1016/j.cden.2017.08.007. PubMed PMID: 29126497.

Zhang WB, Peng X. Cervical metastases of oral maxillary squamous cell carcinoma: A systematic review and meta-analysis. Head & neck. 2016;38 Suppl 1:E2335-42. Epub 2016/02/19. doi: https://doi.org/10.1002/hed.24274. PubMed PMID: 26890607.

Vu A, Farah CS. Narrow band imaging: clinical applications in oral and oropharyngeal cancer. Oral diseases. 2016;22(5):383-90. Epub 2015/12/30. doi: https://doi.org/10.1111/odi.12430. PubMed PMID: 26713751.

1.1.6.1. Squamous cell carcinoma with variants of oral cavity

1.1.6.2. Squamous cell carcinoma with variants of lip

1.1.7. Epithelial tumours of eye and adnexa

Ford J, Thakar S, Thuro B, Esmaeli B. Prognostic Value of the Staging System for Eyelid Tumors in the 7th Edition of the American Joint Committee on Cancer Staging Manual. Ophthalmic plastic and reconstructive surgery. 2017;33(5):317-24. Epub 2017/03/30. doi: https://doi.org/10.1097/iop.0000000000000901. PubMed PMID: 28350693.

Rico G, Smith SV, Siddiqui Y, Whyte A, Gombos D, Lee AG. Neuro-ophthalmologic manifestations of cholangiocarcinoma: a case series. Eye (London, England). 2017;31(8):1245-8. Epub 2017/05/13. doi: https://doi.org/10.1038/eye.2017.77. PubMed PMID: 28498375; PubMed Central PMCID: PMCPmc5558232.

Silverman N, Shinder R. What's New in Eyelid Tumors. Asia-Pacific journal of ophthalmology (Philadelphia, Pa). 2017;6(2):143-52. Epub 2017/04/12. doi: https://doi.org/10.22608/apo.201701. PubMed PMID: 28399340.

Viani GA, Fendi LI. Adjuvant treatment or primary topical monotherapy for ocular surface squamous neoplasia: a systematic review. Arquivos brasileiros de oftalmologia. 2017;80(2):131-6. Epub 2017/06/08. doi: https://doi.org/10.5935/0004-2749.20170032. PubMed PMID: 28591290.

Zhang M, Fathy C, Breazzano MP, Hollar M, Barahimi B. Intra-arterial Chemotherapy for Lacrimal Gland Adenoid Cystic Carcinoma. International ophthalmology clinics. 2017;57(1):143-52. Epub 2016/11/30. doi: https://doi.org/10.1097/iio.0000000000000158. PubMed PMID: 27898620.

1.1.7.1. Squamous cell carcinoma with variants of eye and adnexa

1.1.7.2. Adenocarcinoma with variants of eye and adnexa

1.1.8. Epithelial tumours of middle ear

Cugley DR, Roberts-Thomson SJ, McNab AA, Pick Z. Biopsy-Proven Metastatic Merkel Cell Carcinoma to the Orbit: Case Report and Review of Literature. Ophthalmic plastic and reconstructive surgery. 2018;34(3):e86-e8. Epub 2018/03/06. doi: https://doi.org/10.1097/iop.0000000000001078. PubMed PMID: 29505467.

Nader ME, Bell D, Ginsberg L, DeMonte F, Gunn GB, Gidley PW. The First Reported Case of Primary Intestinal-type Adenocarcinoma of the Middle Ear and Review of the Literature. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2017;38(9):e364-e8. Epub 2017/08/11. doi: https://doi.org/10.1097/mao.0000000000001541. PubMed PMID: 28796082.

Uccella S, Ottini G, Facco C, Maragliano R, Asioli S, Sessa F, et al. Neuroendocrine neoplasms of the head and neck and olfactory neuroblastoma. Diagnosis and classification. Pathologica. 2017;109(1):14-30. Epub 2017/06/22. PubMed PMID: 28635990.

Yang Y, Zhou J, Wu H. Diagnostic value of sentinel lymph node biopsy for cT1/T2N0 tongue squamous cell carcinoma: a meta-analysis. European archives of oto-rhino-laryngology : official journal of the European

Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2017;274(11):3843-52. Epub 2017/09/14. doi: https://doi.org/10.1007/s00405-017-4740-3. PubMed PMID: 28900723.

Caroppo D, Salerno G, Merolla F, Mesolella M, Ilardi G, Pagliuca F, et al. Coexistent Squamous Cell Carcinoma and Granular Cell Tumor of Head and Neck Region: Report of Two Very Rare Cases and Review of the Literature. International journal of surgical pathology. 2018;26(1):47-51. Epub 2017/08/09. doi: https://doi.org/10.1177/1066896917724513. PubMed PMID: 28783989.

1.1.8.1. Squamous cell carcinoma with variants middle ear

1.1.8.2. Adenocarcinoma with variants of middle ear

1.2. Thoracic rare cancers

1.2.1. Epithelial tumour of trachea

1.2.1.1. Squamous cell carcinoma with variants of trachea

Moores D, Mane P. Pathology of Primary Tracheobronchial Malignancies Other than Adenoid Cystic Carcinomas. Thoracic surgery clinics. 2018;28(2):149-54. Epub 2018/04/09. doi: https://doi.org/10.1016/j.thorsurg.2018.01.003. PubMed PMID: 29627048.

Barauna Neto JC, Dedivitis RA, Aires FT, Pfann RZ, Matos LL, Cernea CR. Comparison between Primary and Secondary Tracheoesophageal Puncture Prosthesis: A Systematic Review. ORL; journal for oto-rhino-laryngology and its related specialties. 2017;79(4):222-9. Epub 2017/08/03. doi: https://doi.org/10.1159/000477970. PubMed PMID: 28768272.

Barczak W, Golusinski P, Luczewski L, Suchorska WM, Masternak MM, Golusinski W. The importance of stem cell engineering in head and neck oncology. Biotechnology letters. 2016;38(10):1665-72. Epub 2016/06/28. doi: https://doi.org/10.1007/s10529-016-2163-7.

Hoeben A, Polak J, Van De Voorde L, Hoebers F, Grabsch HI, de Vos-Geelen J. Cervical esophageal cancer: a gap in cancer knowledge. Annals of oncology : official journal of the European Society for Medical Oncology. 2016;27(9):1664-74. Epub 2016/04/28. doi: https://doi.org/10.1093/annonc/mdw183. PubMed PMID: 27117535.

Herbella FA, Neto SP, Santoro IL, Figueiredo LC. Gastroesophageal reflux disease and non-esophageal cancer. World journal of gastroenterology. 2015;21(3):815-9. Epub 2015/01/28. doi: https://doi.org/10.3748/wjg.v21.i3.815. PubMed PMID: 25624714; PubMed Central PMCID: PMCPmc4299333.

1.2.1.2. Adenocarcinoma with variants of trachea

Maziak DE. Biology of Adenoid Cystic Carcinoma of the Tracheobronchial Tree and Principles of Management. Thoracic surgery clinics. 2018;28(2):145-8. Epub 2018/04/09. doi: https://doi.org/10.1016/j.thorsurg.2018.01.002. PubMed PMID: 29627047.

Shirian S, Maghbool M, Aledavood A, Negahban S, Khademi B, Daneshbod Y. Adenoid Cystic Carcinoma of the Larynx Presenting as a Thyroid Mass and Brief Literature Review. Acta cytologica. 2017;61(3):237-41. Epub 2017/05/11. doi: https://doi.org/10.1159/000464271. PubMed PMID: 28490006.

Varela P, Pio L, Torre M. Primary tracheobronchial tumors in children. Seminars in pediatric surgery. 2016;25(3):150-5. Epub 2016/06/16. doi: https://doi.org/10.1053/j.sempedsurg.2016.02.013. PubMed PMID: 27301601.

Elktaibi A, Elhammoumi M, Boudhas A, Arsalane A, Eloueriachi F, Oukabli M, et al. Adenoid cystic carcinoma of the trachea: a clinico-pathological analysis. The Pan African medical journal. 2015;20:240. Epub

2015/01/01. doi: https://doi.org/10.11604/pamj.2015.20.240.3953. PubMed PMID: 27386036; PubMed Central PMCID: PMCPmc4919678.

Desai HM, Thakare R, Amonkar GP, Karkhanis V, Joshi JM. Adenoid cystic carcinoma of the trachea. Indian journal of pathology & microbiology. 2015;58(4):516-8. Epub 2015/11/10. doi: https://doi.org/10.4103/0377-4929.168889. PubMed PMID: 26549080.

1.2.1.3. Salivary gland type tumours of trachea

Moores D, Mane P. Pathology of Primary Tracheobronchial Malignancies Other than Adenoid Cystic Carcinomas. Thoracic surgery clinics. 2018;28(2):149-54. Epub 2018/04/09. doi: https://doi.org/10.1016/j.thorsurg.2018.01.003. PubMed PMID: 29627048.

Desai HM, Thakare R, Amonkar GP, Karkhanis V, Joshi JM. Adenoid cystic carcinoma of the trachea. Indian journal of pathology & microbiology. 2015;58(4):516-8. Epub 2015/11/10. doi: https://doi.org/10.4103/0377-4929.168889. PubMed PMID: 26549080.

1.2.2. Rare epithelial tumours of lung

1.2.2.1. Adenosquamous carcinoma of lung

Guo LC, Li G, Wang XM, Zhang M, Huang JA, Chen YB. Penile metastases from primary lung cancer: Case report and literature review. Medicine. 2017;96(26):e7307. Epub 2017/06/29. doi: https://doi.org/10.1097/md.0000000000007307. PubMed PMID: 28658136; PubMed Central PMCID: PMCPmc5500058.

Hou S, Zhou S, Qin Z, Yang L, Han X, Yao S, et al. Evidence, Mechanism, and Clinical Relevance of the Transdifferentiation from Lung Adenocarcinoma to Squamous Cell Carcinoma. The American journal of pathology. 2017;187(5):954-62. Epub 2017/03/13. doi: https://doi.org/10.1016/j.ajpath.2017.01.009. PubMed PMID: 28284717.

Cho HJ, Kim HR, Park YS, Kim YH, Kim DK, Park SI. Prognostic value of survivin expression in stage III non-small cell lung cancer patients treated with platinum-based therapy. Surgical oncology. 2015;24(4):329-34. Epub 2015/12/23. doi: https://doi.org/10.1016/j.suronc.2015.09.001. PubMed PMID: 26690822.

Rao N. Adenosquamous carcinoma. Seminars in diagnostic pathology. 2014;31(4):271-7. Epub 2014/07/09. doi: https://doi.org/10.1053/j.semdp.2014.06.004. PubMed PMID: 25002356.

Glass R, Hukku SR, Gershenhorn B, Alzate J, Tan B. Metastasis of lung adenosquamous carcinoma to meningioma: case report with literature review. International journal of clinical and experimental pathology. 2013;6(11):2625-30. Epub 2013/11/15. PubMed PMID: 24228131; PubMed Central PMCID: PMCPmc3816838.

1.2.2.2 Large cell carcinoma of lung

Ali RH, Taraboanta C, Mohammad T, Hayes MM, Ionescu DN. Metastatic non-small cell lung carcinoma a mimic of primary breast carcinoma-case series and literature review. Virchows Archiv : an international journal of pathology. 2018;472(5):771-7. Epub 2017/11/07. doi: https://doi.org/10.1007/s00428-017-2262-4. PubMed PMID: 29105026.

Brinkmeyer JK, Moore DC. Necitumumab for the treatment of squamous cell non-small cell lung cancer. Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners. 2018;24(1):37-41. Epub 2016/12/04. doi: https://doi.org/10.1177/1078155216682365. PubMed PMID: 27913776.

Francolini G, Ferrari K, Scotti V. Neoadjuvant approach for nonsmall cell lung cancer: overview of the current issues. Current opinion in oncology. 2017;29(2):123-8. Epub 2016/12/28. doi: https://doi.org/10.1097/cco.0000000000000354. PubMed PMID: 28027103.

Broodman I, Lindemans J, van Sten J, Bischoff R, Luider T. Serum Protein Markers for the Early Detection of Lung Cancer: A Focus on Autoantibodies. Journal of proteome research. 2017;16(1):3-13. Epub 2016/10/23. doi: https://doi.org/10.1021/acs.jproteome.6b00559. PubMed PMID: 27769114.

de Baere T, Tselikas L, Catena V, Buy X, Deschamps F, Palussiere J. Percutaneous thermal ablation of primary lung cancer. Diagnostic and interventional imaging. 2016;97(10):1019-24. Epub 2016/10/04. doi: https://doi.org/10.1016/j.diii.2016.08.016. PubMed PMID: 27692673.

1.2.2.3. Salivary gland type tumours of lung

Moores D, Mane P. Pathology of Primary Tracheobronchial Malignancies Other than Adenoid Cystic Carcinomas. Thoracic surgery clinics. 2018;28(2):149-54. Epub 2018/04/09. doi: https://doi.org/10.1016/j.thorsurg.2018.01.003. PubMed PMID: 29627048.

Kalhor N, Weissferdt A, Moran CA. Primary Salivary Gland Type Tumors of the Thymus. Advances in anatomic pathology. 2017;24(1):15-23. Epub 2016/12/13. doi: https://doi.org/10.1097/pap.0000000000000132. PubMed PMID: 27941539.

Salem A, Bell D, Sepesi B, Papadimitrakopoulou V, El-Naggar A, Moran CA, et al. Clinicopathologic and genetic features of primary bronchopulmonary mucoepidermoid carcinoma: the MD Anderson Cancer Center experience and comprehensive review of the literature. Virchows Archiv : an international journal of pathology. 2017;470(6):619-26. Epub 2017/03/28. doi: https://doi.org/10.1007/s00428-017-2104-4. PubMed PMID: 28343305.

Zhang XP, Jiang GY, Zhang QF, Xu HT, Li QC, Wang EH. Primary acinic cell carcinoma of the lung with psammoma bodies: A case report and review of literature. Pathology, research and practice. 2017;213(4):405-9. Epub 2017/02/19. doi: https://doi.org/10.1016/j.prp.2017.01.011. PubMed PMID: 28214199.

Falk N, Weissferdt A, Kalhor N, Moran CA. Primary Pulmonary Salivary Gland-type Tumors: A Review and Update. Advances in anatomic pathology. 2016;23(1):13-23. Epub 2015/12/10. doi: https://doi.org/10.1097/pap.0000000000000099. PubMed PMID: 26645458.

1.2.2.4. Sarcomatoid carcinoma of lung

Le Caer H, Teissier E, Barriere JR, Venissac N. Classic biphasic pulmonary blastoma: A case report and review of the literature. Critical reviews in oncology/hematology. 2018;125:48-50. Epub 2018/04/14. doi: https://doi.org/10.1016/j.critrevonc.2018.02.009. PubMed PMID: 29650276.

Kim H, Park YW, Oh YH, Sim J, Ro JY, Pyo JY. Anaplastic Transformation of Papillary Thyroid Carcinoma Only Seen in Pleural Metastasis: A Case Report with Review of the Literature. Head and neck pathology. 2017;11(2):162-7. Epub 2016/08/24. doi: https://doi.org/10.1007/s12105-016-0751-4. PubMed PMID: 27550513; PubMed Central PMCID: PMCPmc5429274.

Cho MH, Kim SH, Park WS, Joung JY, Seo HK, Chung J, et al. Bladder chondrosarcoma plus urothelial carcinoma in recurred transitional cell carcinoma of the upper urinary tract: a case report and literature review. World journal of surgical oncology. 2016;14(1):270. Epub 2016/10/22. doi: https://doi.org/10.1186/s12957-016-1021-3. PubMed PMID: 27765044; PubMed Central PMCID: PMCPmc5073732.

Pelosi G, Scarpa A, Forest F, Sonzogni A. The impact of immunohistochemistry on the classification of lung tumors. Expert review of respiratory medicine. 2016;10(10):1105-21. Epub 2016/09/13. doi: https://doi.org/10.1080/17476348.2017.1235975. PubMed PMID: 27617475.

Xu X, Lin M, Wang S, Jin Z, Han S, Liu X, et al. Lung Sarcomatoid Carcinoma Metastasis to Skin: A Case Report and Review of the Literature. Cancer investigation. 2016;34(6):286-92. Epub 2016/06/28. doi: https://doi.org/10.1080/07357907.2016.1193744. PubMed PMID: 27348718.

1.2.3. Epithelial tumours of thymus

1.2.3.1 Malignant thymoma

Carter BW, Lichtenberger JP, 3rd, Benveniste MF. MR Imaging of Thymic Epithelial Neoplasms. Topics in magnetic resonance imaging : TMRI. 2018;27(2):65-71. Epub 2018/04/04. doi: https://doi.org/10.1097/rmr.0000000000000160. PubMed PMID: 29613961.

Nakada T, Akiba T, Yabe M, Tanaka K, Nakano M, Suzuki M, et al. Clinicopathological Features of Thymoma with Ring Calcification: Case Reports. Annals of thoracic and cardiovascular surgery : official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia. 2017;23(5):256-61. Epub 2017/05/02. doi: https://doi.org/10.5761/atcs.cr.16-00247. PubMed PMID: 28458302; PubMed Central PMCID: PMCPmc5655338.

Scorsetti M, Leo F, Trama A, D'Angelillo R, Serpico D, Macerelli M, et al. Thymoma and thymic carcinomas. Critical reviews in oncology/hematology. 2016;99:332-50. Epub 2016/01/29. doi: https://doi.org/10.1016/j.critrevonc.2016.01.012. PubMed PMID: 26818050.

Zhao L, Zhou X, Li Z, Liu Y. Bone metastasis of malignant thymomas associated with peripheral T-cell lymphocytosis. BMC surgery. 2016;16(1):58. Epub 2016/08/21. doi: https://doi.org/10.1186/s12893-016-0171-0. PubMed PMID: 27542926; PubMed Central PMCID: PMCPmc4992230.

Luo T, Zhao H, Zhou X. The clinical features, diagnosis and management of recurrent thymoma. Journal of cardiothoracic surgery. 2016;11(1):140. Epub 2016/09/02. doi: https://doi.org/10.1186/s13019-016-0533-9. PubMed PMID: 27580949; PubMed Central PMCID: PMCPmc5007840.

1.2.3.2. Squamous cell carcinoma of thymus

Koyama S, Nakamura Y, Yokoyama Y, Morisaki T, Fukuhara T, Fujiwara K, et al. Basaloid squamous cell carcinoma arising in an inverted papilloma in the nasal cavity: A case report and review. Auris, nasus, larynx. 2017;44(5):624-8. Epub 2016/10/11. doi: https://doi.org/10.1016/j.anl.2016.09.005. PubMed PMID: 27720480.

Salmaninejad A, Zamani MR, Pourvahedi M, Golchehre Z, Hosseini Bereshneh A, Rezaei N. Cancer/Testis Antigens: Expression, Regulation, Tumor Invasion, and Use in Immunotherapy of Cancers. Immunological investigations. 2016;45(7):619-40. Epub 2016/09/08. doi: https://doi.org/10.1080/08820139.2016.1197241. PubMed PMID: 27603913.

Marx A, Chan JK, Coindre JM, Detterbeck F, Girard N, Harris NL, et al. The 2015 World Health Organization Classification of Tumors of the Thymus: Continuity and Changes. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2015;10(10):1383-95. Epub 2015/08/22. doi: https://doi.org/10.1097/jto.0000000000000654. PubMed PMID: 26295375; PubMed Central PMCID: PMCPmc4581965.

Sasaki S, Fukushima T, Maruyama Y, Gomi D, Kobayashi T, Sekiguchi N, et al. Two Cases of Thymic Carcinoma Initially Presenting as Bone Metastasis: A Clinical Report and the Usefulness of CD5 Immunohistochemistry for Assessing Bone Lesions. Internal medicine (Tokyo, Japan). 2015;54(14):1781-5. Epub 2015/07/17. doi: https://doi.org/10.2169/internalmedicine.54.4250. PubMed PMID: 26179536.

1.2.3.3. Undifferentiated carcinoma of thymus

Carter BW, Lichtenberger JP, 3rd, Benveniste MF. MR Imaging of Thymic Epithelial Neoplasms. Topics in magnetic resonance imaging : TMRI. 2018;27(2):65-71. Epub 2018/04/04. doi: https://doi.org/10.1097/rmr.0000000000000160. PubMed PMID: 29613961.

Hamaji M, Shah RM, Ali SO, Bettenhausen A, Lee HS, Burt BM. A Meta-Analysis of Postoperative Radiotherapy for Thymic Carcinoma. The Annals of thoracic surgery. 2017;103(5):1668-75. Epub 2017/04/04. doi: https://doi.org/10.1016/j.athoracsur.2016.12.042. PubMed PMID: 28366466.

Wong EHC, Tetter N, Tzankov A, Muller L. CASTLE tumor of the parotid: First documented case, literature review, and genetic analysis of the cancer. Head & neck. 2018;40(1):E1-e4. Epub 2017/11/10. doi: https://doi.org/10.1002/hed.24985. PubMed PMID: 29120527.

Weissferdt A, Moran CA. The spectrum of ectopic thymomas. Virchows Archiv : an international journal of pathology. 2016;469(3):245-54. Epub 2016/06/04. doi: https://doi.org/10.1007/s00428-016-1967-0. PubMed PMID: 27255665.

Moser B, Schiefer AI, Janik S, Marx A, Prosch H, Pohl W, et al. Adenocarcinoma of the thymus, enteric type: report of 2 cases, and proposal for a novel subtype of thymic carcinoma. The American journal of surgical pathology. 2015;39(4):541-8. Epub 2014/12/18. doi: https://doi.org/10.1097/pas.0000000000000359. PubMed PMID: 25517960.

1.2.3.4. Lymphoepithelial carcinoma of thymus

1.2.3.5. Adenocarcinoma with variants of thymus

Litvak A, Pietanza MC. Bronchial and Thymic Carcinoid Tumors. Hematology/oncology clinics of North America. 2016;30(1):83-102. Epub 2015/11/29. doi: https://doi.org/10.1016/j.hoc.2015.09.003. PubMed PMID: 26614370.

Mandegaran R, David S, Screaton N. Cardiothoracic manifestations of neuroendocrine tumours. The British journal of radiology. 2016;89(1060):20150787. Epub 2016/01/20. doi: https://doi.org/10.1259/bjr.20150787. PubMed PMID: 26781701; PubMed Central PMCID: PMCPmc4846207.

Falk NK, Weissferdt A, Habra MA, Roy-Chowdhuri S. Adrenocorticotropic hormone-producing thymic neuroendocrine carcinoma with oncocytic features: a case report and review of literature. Diagnostic cytopathology. 2015;43(4):329-34. Epub 2014/10/31. doi: https://doi.org/10.1002/dc.23209. PubMed PMID: 25354884.

Moser B, Schiefer AI, Janik S, Marx A, Prosch H, Pohl W, et al. Adenocarcinoma of the thymus, enteric type: report of 2 cases, and proposal for a novel subtype of thymic carcinoma. The American journal of surgical pathology. 2015;39(4):541-8. Epub 2014/12/18. doi: https://doi.org/10.1097/pas.0000000000000359. PubMed PMID: 25517960.

Wang L, Wang D, Qian K, Lu D, Chen L, Zhao L, et al. Thymic adenocarcinoma associated with thymic cyst: a case report and review of literature. International journal of clinical and experimental pathology. 2015;8(5):5890-5. Epub 2015/07/21. PubMed PMID: 26191314; PubMed Central PMCID: PMCPmc4503185.

1.2.4. Malignant mesothelioma

1.2.4.1. Mesothelioma of pleura and pericardium

Carter BW, Betancourt SL, Shroff GS, Lichtenberger JP, 3rd. MR Imaging of Pleural Neoplasms. Topics in magnetic resonance imaging : TMRI. 2018;27(2):73-82. Epub 2018/04/04. doi: https://doi.org/10.1097/rmr.0000000000000162. PubMed PMID: 29613962.

Chen F, Liu B, Yu Y, Du J, Chen D. Primary Spinal Malignant Mesothelioma: A Case Report and Literature Review. World neurosurgery. 2018;114:211-6. Epub 2018/03/29. doi: https://doi.org/10.1016/j.wneu.2018.03.124. PubMed PMID: 29588242.

Guazzelli A, Bakker E, Tian K, Demonacos C, Krstic-Demonacos M, Mutti L. Promising investigational drug candidates in phase I and phase II clinical trials for mesothelioma. Expert opinion on investigational drugs. 2017;26(8):933-44. Epub 2017/07/07. doi: https://doi.org/10.1080/13543784.2017.1351545. PubMed PMID: 28679291.

Arnold DT, Clive AO. Prophylactic radiotherapy for procedure tract metastases in mesothelioma: a review. Current opinion in pulmonary medicine. 2017;23(4):357-64. Epub 2017/04/21. doi: https://doi.org/10.1097/mcp.0000000000000385. PubMed PMID: 28426469.

Ashton M, O'Rourke N, Currie S, Rimner A, Chalmers A. The role of radical radiotherapy in the management of malignant pleural mesothelioma: A systematic review. Radiotherapy and oncology: journal of the European Society for Therapeutic Radiology and Oncology. 2017;125(1):1-12. Epub 2017/09/02. doi: https://doi.org/10.1016/j.radonc.2017.08.003. PubMed PMID: 28859932; PubMed Central PMCID: PMCPmc5792070.

1.2.4.2. Mesothelioma of peritoneum and tunica vaginalis

Chen F, Liu B, Yu Y, Du J, Chen D. Primary Spinal Malignant Mesothelioma: A Case Report and Literature Review. World neurosurgery. 2018;114:211-6. Epub 2018/03/29. doi: https://doi.org/10.1016/j.wneu.2018.03.124. PubMed PMID: 29588242.

Mezei G, Chang ET, Mowat FS, Moolgavkar SH. Epidemiology of mesothelioma of the pericardium and tunica vaginalis testis. Annals of epidemiology. 2017;27(5):348-59.e11. Epub 2017/05/22. doi: https://doi.org/10.1016/j.annepidem.2017.04.001. PubMed PMID: 28527639.

Mrinakova B, Kajo K, Ondrusova M, Simo J, Ondrus D. Malignant Mesothelioma of the Tunica Vaginalis Testis. A Clinicopathologic Analysis of Two Cases with a Review of the Literature. Klinicka onkologie : casopis Ceske a Slovenske onkologicke spolecnosti. 29(5):369-74. Epub 2016/10/16. PubMed PMID: 27739317.

Segura-Gonzalez M, Urias-Rocha J, Castelan-Pedraza J. Malignant Mesothelioma of the Tunica Vaginalis: A Rare Neoplasm—Case Report and Literature Review. Clinical genitourinary cancer. 2015;13(6):e401-5. Epub 2015/06/28. doi: https://doi.org/10.1016/j.clgc.2015.05.009. PubMed PMID: 26116329.

Zhang CH, Yu JW, Luo M. Multicystic peritoneal mesothelioma: A short review. Current problems in cancer. 2017;41(5):340-8. Epub 2017/05/22. doi: https://doi.org/10.1016/j.currproblcancer.2017.03.002. PubMed PMID: 28528021.

1.3. Male genital and urogenital rare cancers

1.3.1. Rare epithelial tumours of prostate

1.3.1.1. Squamous cell carcinoma with variants of prostate

1.3.1.2. Infiltrating duct carcinoma of prostate

Seipel AH, Whitington T, Delahunt B, Samaratunga H, Mayrhofer M, Wiklund P, et al. Genetic profile of ductal adenocarcinoma of the prostate. Hum Pathol. 2017;69:1-7. Epub 2017/04/27. doi: https://doi.org/10.1016/j.humpath.2017.04.015. PubMed PMID: 28457729.

1.3.1.3. Transitional cell carcinoma of prostate

1.3.1.4. Salivary gland type tumours of prostate

1.3.2. Testicular and paratesticular cancers

1.3.2.1. Paratesticular adenocarcinoma with variants

Wick MR. Primary lesions that may imitate metastatic tumors histologically: A selective review. Semin Diagn Pathol. 2018;35(2):123-42. Epub 2017/11/17. doi: https://doi.org/10.1053/j.semdp.2017.11.010. PubMed PMID: 29174934.

Zou ZJ, Xiao YM, Liu ZH, Zhang RC, Liang JY, Tang YQ, et al. Clinicopathological Characteristics, Treatment, and Prognosis of Rarely Primary Epididymal Adenocarcinoma: A Review and Update. Biomed Res Int. 2017;2017:4126740. Epub 2017/12/20. doi: https://doi.org/10.1155/2017/4126740. PubMed PMID: 29423406; PubMed Central PMCID: PMCPMC5750466.

1.3.2.2. Non seminomatous testicular cancer

Stall JN, Young RH. Polyembryoma of the testis: a report of two cases dominant within mixed germ cell tumors and review of gonadal polyembryomas. Mod Pathol. 2017;30(7):908-18. Epub 2017/04/21. doi: https://doi.org/10.1038/modpathol.2017.25. PubMed PMID: 28429716.

Hoffman HA, Toshkezi G, Fullmer JM, Hall W, Chin LS. Pitfalls in Diagnosis and Management of Testicular Choriocarcinoma Metastatic to the Brain: Report of 2 Cases and Review of Literature. World Neurosurg. 2017;106:536-42. Epub 2017/07/13. doi: https://doi.org/10.1016/j.wneu.2017.07.023. PubMed PMID: 28712904.

Takada H, Iwatsuki S, Itoh Y, Sato S, Hayase M, Yasui T. Primary pure carcinoid tumour of the testis: A case report and review of the literature. Arch Ital Urol Androl. 2016;88(3):245-6. Epub 2016/10/05. doi: https://doi.org/10.4081/aiua.2016.3.245. PubMed PMID: 27711107.

Lubana SS, Singh N, Chan HC, Heimann D. Primary neuroendocrine tumor (carcinoid tumor) of the testis: a case report with review of literature. Am J Case Rep. 2015;16:328-32. Epub 2015/05/31. doi: https://doi.org/10.12659/ajcr.894463. PubMed PMID: 26027014; PubMed Central PMCID: PMCPMC4463997.

Reilley MJ, Pagliaro LC. Testicular choriocarcinoma: a rare variant that requires a unique treatment approach. Curr Oncol Rep. 2015;17(2):2. doi: https://doi.org/10.1007/s11912-014-0430-0. PubMed PMID: 25645112.

1.3.2.3. Seminomatous testicular cancer

Palicelli A, Neri P, Marchioro G, De Angelis P, Bondonno G, Ramponi A. Paratesticular seminoma: echographic features and histological diagnosis with review of the literature. APMIS. 2018;126(3):267-72. Epub 2018/02/07. doi: https://doi.org/10.1111/apm.12806. PubMed PMID: 29411910.

Marko J, Wolfman DJ, Aubin AL, Sesterhenn IA. Testicular Seminoma and Its Mimics: From the Radiologic Pathology Archives. Radiographics. 2017;37(4):1085-98. Epub 2017/06/02. doi: https://doi.org/10.1148/rg.2017160164. PubMed PMID: 28574809; PubMed Central PMCID: PMCPMC5548453.

Yathiraj PH, Sharan K, Fernandes DJ, Vidyasagar MS. Adjuvant treatment for Stage I seminoma: Why radiotherapy is better than carboplatin. J Cancer Res Ther. 2016;12(4):1216-9. doi: https://doi.org/10.4103/0973-1482.176171. PubMed PMID: 28169230.

Pearce SM, Liauw SL, Eggener SE. Management of Low-Stage Testicular Seminoma. Urol Clin North Am. 2015;42(3):287-98. Epub 2015/06/06. doi: https://doi.org/10.1016/j.ucl.2015.04.003. PubMed PMID: 26216816.

Giannatempo P, Greco T, Mariani L, Nicolai N, Tana S, Farè E, et al. Radiotherapy or chemotherapy for clinical stage IIA and IIB seminoma: a systematic review and meta-analysis of patient outcomes. Ann Oncol. 2015;26(4):657-68. Epub 2014/09/11. doi: https://doi.org/10.1093/annonc/mdu447. PubMed PMID: 25214543.

1.3.2.4. Spermatocytic seminoma

Gentile G, Giunchi F, Schiavina R, Franceschelli A, Borghesi M, Zukerman Z, et al. First case of bilateral, synchronous anaplastic variant of spermatocytic seminoma treated with radical orchifunicolectomy as

single approach: case report and review of the literature. Arch Ital Urol Androl. 2014;86(1):41-2. Epub 2014/03/28. doi: https://doi.org/10.4081/aiua.2014.1.41. PubMed PMID: 24704931.

Mikuz G. [Spermatocytic seminoma. A tumor with many faces]. Pathologe. 2014;35(3):232-7. doi: https://doi.org/10.1007/s00292-014-1899-x. PubMed PMID: 24682373.

1.3.2.5. Teratoma with malignant transformation

Silván U, Díez-Torre A, Bonilla Z, Moreno P, Díaz-Núñez M, Aréchaga J. Vasculogenesis and angiogenesis in nonseminomatous testicular germ cell tumors. Urol Oncol. 2015;33(6):268.e17-28. Epub 2015/03/12. doi: https://doi.org/10.1016/j.urolonc.2015.01.005. PubMed PMID: 25772688.

Cabral FC, Krajewski KM, Rosenthal MH, Hirsch MS, Howard SA. Teratoma with malignant transformation: report of three cases and review of the literature. Clin Imaging. 2014;38(5):589-93. Epub 2014/04/28. doi: https://doi.org/10.1016/j.clinimag.2014.04.011. PubMed PMID: 24908364.

1.3.2.6. Testicular sex cord cancer

Roth LM, Cheng L. Classical gonadoblastoma: its relationship to the 'dissecting' variant and undifferentiated gonadal tissue. Histopathology. 2018;72(4):545-55. Epub 2017/11/09. doi: https://doi.org/10.1111/his.13387. PubMed PMID: 28881049.

Elbachiri M, Taleb A, Derrabi N, Bouchbika Z, Benchakroun N, Jouhadi H, et al. Adult-type granulosa cell tumor of the testis: report of a case and review of literature. Pan Afr Med J. 2017;26:198. Epub 2017/04/04. doi: https://doi.org/10.11604/pamj.2017.26.198.11523. PubMed PMID: 28674591; PubMed Central PMCID: PMCPMC5483374.

Roth LM, Lyu B, Cheng L. Perspectives on testicular sex cord-stromal tumors and those composed of both germ cells and sex cord-stromal derivatives with a comparison to corresponding ovarian neoplasms. Hum Pathol. 2017;65:1-14. Epub 2017/04/23. doi: https://doi.org/10.1016/j.humpath.2017.04.009. PubMed PMID: 28445692.

Rove KO, Maroni PD, Cost CR, Fairclough DL, Giannarini G, Harris AK, et al. Pathologic Risk Factors for Metastatic Disease in Postpubertal Patients With Clinical Stage I Testicular Stromal Tumors. Urology. 2016;97:138-44. Epub 2016/08/15. doi: https://doi.org/10.1016/j.urology.2016.06.066. PubMed PMID: 27538802.

Rove KO, Maroni PD, Cost CR, Fairclough DL, Giannarini G, Harris AK, et al. Pathologic Risk Factors in Pediatric and Adolescent Patients With Clinical Stage I Testicular Stromal Tumors. J Pediatr Hematol Oncol. 2015;37(8):e441-6. doi: https://doi.org/10.1097/mph.0000000000000445. PubMed PMID: 26479987.

1.3.3. Epithelial tumours of penis

1.3.3.1. Squamous cell carcinoma with variants of penis

Erbersdobler A. Pathologic Evaluation and Reporting of Carcinoma of the Penis. Clin Genitourin Cancer. 2017;15(2):192-5. Epub 2016/08/10. doi: https://doi.org/10.1016/j.clgc.2016.08.003. PubMed PMID: 27594553.

Crook J. Contemporary Role of Radiotherapy in the Management of Primary Penile Tumors and Metastatic Disease. Urol Clin North Am. 2016;43(4):435-48. doi: https://doi.org/10.1016/j.ucl.2016.06.005. PubMed PMID: 27717430.

Downes MR. Review of in situ and invasive penile squamous cell carcinoma and associated non-neoplastic dermatological conditions. J Clin Pathol. 2015;68(5):333-40. doi: https://doi.org/10.1136/jclinpath-2015-202911. PubMed PMID: 25883161.

Lau WD, Ong CH, Lim TP, Teo C. Penile cancer: a local case series and literature review. Singapore Med J. 2015;56(11):637-40. doi: https://doi.org/10.11622/smedj.2015174. PubMed PMID: 26668410; PubMed Central PMCID: PMCPMC4656873.

Pagliaro LC. Role of chemotherapy in treatment of squamous cell carcinoma of the penis. Curr Probl Cancer. 2015;39(3):166-72. Epub 2015/03/31. doi: https://doi.org/10.1016/j.currproblcancer.2015.03.008. PubMed PMID: 25920379.

1.3.3.2. Adenocarcinoma with variants of penis

Rush PS, Shiau JM, Hibler BP, Longley BJ, Downs TM, Bennett DD. Primary cutaneous adenosquamous carcinoma of the penis: the first characterization of HPV status in this rare and diagnostically challenging entity with review of glandular carcinomas of the penis. J Cutan Pathol. 2016;43(12):1226-30. doi: https://doi.org/10.1111/cup.12835. PubMed PMID: 27696488.

1.3.4. Rare epithelial tumours of kidney

1.3.4.1. Squamous cell carcinoma spindle cell type of kidney

1.3.4.2. Squamous cell carcinoma with variants of kidney

Jiang P, Wang C, Chen S, Li J, Xiang J, Xie L. Primary renal squamous cell carcinoma mimicking the renal cyst: a case report and review of the recent literature. BMC Urol. 2015;15:69. Epub 2015/07/23. doi: https://doi.org/10.1186/s12894-015-0064-z. PubMed PMID: 26201315; PubMed Central PMCID: PMCPMC4511242.

1.3.5. Epithelial tumours of pelvis and ureter

1.3.5.1. Transitional cell carcinoma of pelvis and ureter

Li M, Shi A, Kong W, Zhang J, Chen Y, Huang J, et al. Transitional cell carcinoma with extension of the renal vein and IVC tumor thrombus: report of three cases and literature review. World J Surg Oncol. 2016;14(1):309. Epub 2016/12/28. doi: https://doi.org/10.1186/s12957-016-1041-z. PubMed PMID: 28031042; PubMed Central PMCID: PMCPMC5192594.

Lucarelli G, Spilotros M, Vavallo A, Palazzo S, Miacola C, Forte S, et al. A Challenging Surgical Approach to Locally Advanced Primary Urethral Carcinoma: A Case Report and Literature Review. Medicine (Baltimore). 2016;95(19):e3642. doi: https://doi.org/10.1097/md.0000000000003642. PubMed PMID: 27175683; PubMed Central PMCID: PMCPMC4902525.

Traboulsi SL, Witjes JA, Kassouf W. Contemporary Management of Primary Distal Urethral Cancer. Urol Clin North Am. 2016;43(4):493-503. doi: https://doi.org/10.1016/j.ucl.2016.06.010. PubMed PMID: 27717435.

Zinman LN, Vanni AJ. Management of Proximal Primary Urethral Cancer: Should Multidisciplinary Therapy Be the Gold Standard? Urol Clin North Am. 2016;43(4):505-13. doi: https://doi.org/10.1016/j.ucl.2016.06.011. PubMed PMID: 27717436.

Corbishley CM, Rajab RM, Watkin NA. Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol. 2015;32(3):238-44. Epub 2014/12/25. doi: https://doi.org/10.1053/j.semdp.2014.12.015. PubMed PMID: 25656527.

1.3.5.2. Squamous cell carcinoma with variants of pelvis and ureter

Reddy BN, Subhash M, Pilichowska M, Klauber GT. Primary Squamous Cell Carcinoma Arising From a Cutaneous urethraovesical Stoma (Modified Mitrofanoff): Case Report and Review of Literature. Urology. 2017;99:225-7. Epub 2016/06/17. doi: https://doi.org/10.1016/j.urology.2016.06.017. PubMed PMID: 27327575.

Hassan M, Qureshi A, Nasir H. Recurrent verrucous carcinoma of the urinary bladder after transurethral resection followed by intravesical mitomycin, and a review of the literature. BMJ Case Rep. 2016;2016. Epub 2016/06/15. doi: https://doi.org/10.1136/bcr-2016-216146. PubMed PMID: 27307433; PubMed Central PMCID: PMCPMC4932366.

Rausch S, Lotan Y, Youssef RF. Squamous cell carcinogenesis and squamous cell carcinoma of the urinary bladder: a contemporary review with focus on nonbilharzial squamous cell carcinoma. Urol Oncol. 2014;32(1):32.e11-6. Epub 2013/02/20. doi: https://doi.org/10.1016/j.urolonc.2012.11.020. PubMed PMID: 23433891.

1.3.5.3. Adenocarcinoma with variants of pelvis and ureter

Muto M, Inamura K, Ozawa N, Endo T, Masuda H, Yonese J, et al. Skene's gland adenocarcinoma with intestinal differentiation: A case report and literature review. Pathol Int. 2017;67(11):575-9. Epub 2017/09/05. doi: https://doi.org/10.1111/pin.12571. PubMed PMID: 28872768.

Zhang M, Pettaway C, Vikram R, Tamboli P. Adenoid cystic carcinoma of the urethra/Cowper's gland with concurrent high-grade prostatic adenocarcinoma: a detailed clinicopathologic case report and review of the literature. Hum Pathol. 2016;58:138-44. Epub 2016/08/20. doi: https://doi.org/10.1016/j.humpath.2016.07.027. PubMed PMID: 27554206.

Han DS, Yuk SM, Youn CS, Park G, Sul HJ, Jang H. Primary mucinous cystadenocarcinoma of the renal pelvis misdiagnosed as urethraopelvic junction stenosis with renal pelvis stone: a case report and literature review. World J Surg Oncol. 2015;13:324. Epub 2015/11/26. doi: https://doi.org/10.1186/s12957-015-0739-7. PubMed PMID: 26612470; PubMed Central PMCID: PMCPMC4662030.

Venyo AK. Clear cell adenocarcinoma of the urethra: review of the literature. Int J Surg Oncol. 2015;2015:790235. Epub 2015/01/20. doi: https://doi.org/10.1155/2015/790235. PubMed PMID: 25685552; PubMed Central PMCID: PMCPMC4320870.

Sebesta EM, Mirheydar HS, Parsons JK, Wang-Rodriguez J, Kader AK. Primary mucin-producing urothelial-type adenocarcinoma of the prostatic urethra diagnosed on TURP: a case report and review of literature. BMC Urol. 2014;14:39. Epub 2014/05/22. doi: https://doi.org/10.1186/1471-2490-14-39. PubMed PMID: 24885582; PubMed Central PMCID: PMCPMC4059493.

1.3.6. Epithelial tumours of urethra

1.3.6.1. Transitional cell carcinoma of urethra

Li M, Shi A, Kong W, Zhang J, Chen Y, Huang J, et al. Transitional cell carcinoma with extension of the renal vein and IVC tumor thrombus: report of three cases and literature review. World J Surg Oncol. 2016;14(1):309. Epub 2016/12/28. doi: https://doi.org/10.1186/s12957-016-1041-z. PubMed PMID: 28031042; PubMed Central PMCID: PMCPMC5192594.

Lucarelli G, Spilotros M, Vavallo A, Palazzo S, Miacola C, Forte S, et al. A Challenging Surgical Approach to Locally Advanced Primary Urethral Carcinoma: A Case Report and Literature Review. Medicine (Baltimore). 2016;95(19):e3642. doi: https://doi.org/10.1097/md.0000000000003642. PubMed PMID: 27175683; PubMed Central PMCID: PMCPMC4902525.

Traboulsi SL, Witjes JA, Kassouf W. Contemporary Management of Primary Distal Urethral Cancer. Urol Clin North Am. 2016;43(4):493-503. doi: https://doi.org/10.1016/j.ucl.2016.06.010. PubMed PMID: 27717435.

Zinman LN, Vanni AJ. Management of Proximal Primary Urethral Cancer: Should Multidisciplinary Therapy Be the Gold Standard? Urol Clin North Am. 2016;43(4):505-13. doi: https://doi.org/10.1016/j.ucl.2016.06.011. PubMed PMID: 27717436.

Corbishley CM, Rajab RM, Watkin NA. Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol. 2015;32(3):238-44. Epub 2014/12/25. doi: https://doi.org/10.1053/j.semdp.2014.12.015. PubMed PMID: 25656527.

1.3.6.2. Squamous cell carcinoma with variants of urethra

Reddy BN, Subhash M, Pilichowska M, Klauber GT. Primary Squamous Cell Carcinoma Arising From a Cutaneous urethraovesical Stoma (Modified Mitrofanoff): Case Report and Review of Literature. Urology. 2017;99:225-7. Epub 2016/06/17. doi: https://doi.org/10.1016/j.urology.2016.06.017. PubMed PMID: 27327575.

Hassan M, Qureshi A, Nasir H. Recurrent verrucous carcinoma of the urinary bladder after transurethral resection followed by intravesical mitomycin, and a review of the literature. BMJ Case Rep. 2016;2016. Epub 2016/06/15. doi: https://doi.org/10.1136/bcr-2016-216146. PubMed PMID: 27307433; PubMed Central PMCID: PMCPMC4932366.

Rausch S, Lotan Y, Youssef RF. Squamous cell carcinogenesis and squamous cell carcinoma of the urinary bladder: a contemporary review with focus on nonbilharzial squamous cell carcinoma. Urol Oncol. 2014;32(1):32.e11-6. Epub 2013/02/20. doi: https://doi.org/10.1016/j.urolonc.2012.11.020. PubMed PMID: 23433891.

1.3.6.3. Adenocarcinoma with variants of urethra

Zhang M, Pettaway C, Vikram R, Tamboli P. Adenoid cystic carcinoma of the urethra/Cowper's gland with concurrent high-grade prostatic adenocarcinoma: a detailed clinicopathologic case report and review of the literature. Hum Pathol. 2016;58:138-44. Epub 2016/08/20. doi: https://doi.org/10.1016/j.humpath.2016.07.027. PubMed PMID: 27554206.

Venyo AK. Clear cell adenocarcinoma of the urethra: review of the literature. Int J Surg Oncol. 2015;2015:790235. Epub 2015/01/20. doi: https://doi.org/10.1155/2015/790235. PubMed PMID: 25685552; PubMed Central PMCID: PMCPMC4320870.

1.3.7. Rare epithelial tumours of bladder

1.3.7.1. Squamous cell carcinoma with variants of bladder

1.3.7.2. Adenocarcinoma with variants of bladder

Mylonas KS, O Malley P, Ziogas IA, El-Kabab L, Nasioudis D. Malignant urachal neoplasms: A population-based study and systematic review of literature. Urol Oncol. 2017;35(1):33.e11-33.e19. Epub 2016/09/01. doi: https://doi.org/10.1016/j.urolonc.2016.07.021. PubMed PMID: 27592530.

Ozawa M, Kuromoto A, Morozumi K, Satou M, Hoshi S, Numahata K. [Two Cases of Urachal Carcinoma Treated by TS-1/CDDP as Adjuvant Chemotherapy]. Hinyokika Kiyo. 2017;63(10):413-9. PubMed PMID: 29103255.

Ball MW, Nathan R, Gerayli F. Long-Term Response After Surgery and Adjuvant Chemoradiation for T4 Mucinous Adenocarcinoma of the Bladder: A Case Report and Review of the Literature. Clin Genitourin Cancer. 2016;14(2):e225-7. Epub 2015/12/24. doi: https://doi.org/10.1016/j.clgc.2015.12.025. PubMed PMID: 26774348.

Behrendt MA, DE Jong J, VAN Rhijn BW. Urachal cancer: contemporary review of the pathological, surgical, and prognostic aspects of this rare disease. Minerva Urol Nefrol. 2016;68(2):172-84. Epub 2015/11/18. PubMed PMID: 26583595.

Messina C, Dellepiane C, Caroti C, Sarocchi F, Ravetti GL, Boccardo F, et al. A Case of Advanced Mucinous Adenocarcinoma of Bladder in an Adult Patient Treated With Capecitabine-Based Chemotherapy and

Review of Literature. Clin Genitourin Cancer. 2015;13(5):e365-8. Epub 2015/04/15. doi: https://doi.org/10.1016/j.clgc.2015.04.002. PubMed PMID: 25935564.

1.3.7.3. Salivary gland type tumours of bladder

1.3.8. Extragonadal germ cell tumours

Kuo EJ, Sisk AE, Yang Z, Huang J, Yeh MW, Livhits MJ. Adrenal Teratoma: a Case Series and Review of the Literature. Endocr Pathol. 2017;28(2):152-8. doi: https://doi.org/10.1007/s12022-017-9468-5. PubMed PMID: 28091891.

Li Y, Lei C, Xiang B, Li F, Wang C, Wang Q, et al. Extrarenal teratoma with nephroblastoma in the retroperitoneum: Case report and literature review. Medicine (Baltimore). 2017;96(46):e8670. doi: https://doi.org/10.1097/md.0000000000008670. PubMed PMID: 29145295; PubMed Central PMCID: PMCPMC5704840.

Agrawal T, Blau AJ, Chwals WJ, Tischler AS. A Unique Case of Mediastinal Teratoma with Mature Pancreatic Tissue, Nesidioblastosis, and Aberrant Islet Differentiation: a Case Report and Literature Review. Endocr Pathol. 2016;27(1):21-4. doi: https://doi.org/10.1007/s12022-015-9393-4. PubMed PMID: 26318442.

Dasbaksi K, Haldar S, Mukherjee K, Chakraborty U, Majumdar P, Mukherjee P. Intrapulmonary teratoma: Report of a case and review of literature. Asian Cardiovasc Thorac Ann. 2016;24(6):574-7. Epub 2015/05/04. doi: https://doi.org/10.1177/0218492315583763. PubMed PMID: 25939909.

Kakuda M, Matsuzaki S, Kobayashi E, Yoshino K, Morii E, Kimura T. A Case of Extragonadal Teratoma in the Pouch of Douglas and Literature Review. J Minim Invasive Gynecol. 2015;22(7):1311-7. Epub 2015/07/20. doi: https://doi.org/10.1016/j.jmig.2015.07.008. PubMed PMID: 26205577.

1.3.8.1. Non seminomatous germ cell tumours

1.3.8.2. Seminomatous germ cell tumors

1.3.8.3. Germ cell tumors of central nervous system (CNS)

1.4. Female genital rare cancers

1.4.1. Rare epithelial tumours of breast

1.4.1.1. Mammary paget's disease of breast

Dubar S, Boukrid M, Bouquet de Joliniere J, Guillou L, Vo QD, Major A, et al. Paget's Breast Disease: A Case Report and Review of the Literature. Frontiers in surgery. 2017;4:51. doi: https://doi.org/10.3389/fsurg.2017.00051. PubMed PMID: 29109950; PubMed Central PMCID: PMC5660109.

Merrill AY, White A, Howard-McNatt M. Paget's Disease of the Breast: An Institutional Review and Surgical Management. The American surgeon. 2017;83(3):e96-8. PubMed PMID: 28316301.

Adams SJ, Kanthan R. Paget's disease of the male breast in the 21st century: A systematic review. Breast. 2016;29:14-23. doi: https://doi.org/10.1016/j.breast.2016.06.015. PubMed PMID: 27394005.

Helme S, Harvey K, Agrawal A. Breast-conserving surgery in patients with Paget's disease. The British journal of surgery. 2015;102(10):1167-74. doi: https://doi.org/10.1002/bjs.9863. PubMed PMID: 26175231.

Sripathi S, Ayachit A, Kadavigere R, Kumar S, Eleti A, Sraj A. Spectrum of Imaging Findings in Paget's Disease of the Breast-A Pictorial Review. Insights into imaging. 2015;6(4):419-29. doi: https://doi.org/10.1007/s13244-015-0415-z. PubMed PMID: 26142549; PubMed Central PMCID: PMC4519816.

1.4.1.2. Special types of adenocarcinoma of breast

Cheng M, Geng C, Tang T, Song Z. Mucoepidermoid carcinoma of the breast: Four case reports and review of the literature. Medicine. 2017;96(51):e9385. doi: https://doi.org/10.1097/MD.0000000000009385. PubMed PMID: 29390541; PubMed Central PMCID: PMC5758243.

Troxell ML. Merkel cell carcinoma, melanoma, metastatic mimics of breast cancer. Seminars in diagnostic pathology. 2017;34(5):479-95. doi: https://doi.org/10.1053/j.semdp.2017.05.009. PubMed PMID: 28645508.

Ohashi R, Matsubara M, Watarai Y, Yanagihara K, Yamashita K, Tsuchiya S, et al. Diagnostic value of fine needle aspiration and core needle biopsy in special types of breast cancer. Breast cancer. 2016;23(4):675-83. doi: https://doi.org/10.1007/s12282-015-0624-9. PubMed PMID: 26134558.

Dieci MV, Orvieto E, Dominici M, Conte P, Guarneri V. Rare breast cancer subtypes: histological, molecular, and clinical peculiarities. The oncologist. 2014;19(8):805-13. doi: https://doi.org/10.1634/theoncologist.2014-0108. PubMed PMID: 24969162; PubMed Central PMCID: PMC4122475.

1.4.1.3. Metaplastic carcinoma of breast

Alaoui M'hamdi H, Abbad F, Rais H, Asmouki H, Soumani A, Khouchani M, et al. Rare variant of metaplastic carcinoma of the breast: a case report and review of the literature. Journal of medical case reports. 2018;12(1):43. doi: https://doi.org/10.1186/s13256-017-1553-3. PubMed PMID: 29463294; PubMed Central PMCID: PMC5820794.

Donato H, Candelaria I, Oliveira P, Goncalo M, Caseiro-Alves F. Imaging Findings of Metaplastic Carcinoma of the Breast with Pathologic Correlation. Journal of the Belgian Society of Radiology. 2018;102(1):46. doi: https://doi.org/10.5334/jbsr.1386. PubMed PMID: 30039058; PubMed Central PMCID: PMC6032488.

Salemis NS. Metaplastic carcinoma of the breast with mesenchymal differentiation (carcinosarcoma). A unique presentation of an aggressive malignancy and literature review. Breast disease. 2018;37(3):169-75. doi: https://doi.org/10.3233/BD-170313. PubMed PMID: 29504519.

Tran MN, Kleer CG. Matricellular CCN6 (WISP3) protein: a tumor suppressor for mammary metaplastic carcinomas. Journal of cell communication and signaling. 2018;12(1):13-9. doi: https://doi.org/10.1007/s12079-018-0451-9. PubMed PMID: 29357008; PubMed Central PMCID: PMC5842205.

Vellaisamy G, Mohanty S, Rout P, Manjunath S. Metaplastic Carcinoma of Breast and Neurofibromatosis 1: A Rare Association. Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology. 2017;38(3):374-6. doi: https://doi.org/10.4103/ijmpo.ijmpo_7_17. PubMed PMID: 29200695; PubMed Central PMCID: PMC5686988.

1.4.1.4. Salivary gland type tumours of breast

Ngouajio AL, Drejet SM, Phillips DR, Summerlin DJ, Dahl JP. A systematic review including an additional pediatric case report: Pediatric cases of mammary analogue secretory carcinoma. International journal of pediatric otorhinolaryngology. 2017;100:187-93. doi: https://doi.org/10.1016/j.ijporl.2017.07.004. PubMed PMID: 28802370.

Huang S, Liu Y, Su J, Liu J, Guo X, Mei F, et al. „Secretory" Carcinoma of the Skin Mimicking Secretory Carcinoma of the Breast: Case Report and Literature Review. The American Journal of dermatopathology. 2016;38(9):698-703. doi: https://doi.org/10.1097/DAD.0000000000000566. PubMed PMID: 26981741.

Albus J, Batanian J, Wenig BM, Vidal CI. A unique case of a cutaneous lesion resembling mammary analog secretory carcinoma: a case report and review of the literature. The American Journal of dermatopathology. 2015;37(4):e41-4. doi: https://doi.org/10.1097/DAD.0000000000000098. PubMed PMID: 25140660.

Nisa L, Landis BN, Salmina C, Ailianou A, Karamitopoulou E, Giger R. Warthin's tumor of the larynx: a very rare case and systematic review of the literature. Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale. 2015;44:16. doi: https://doi.org/10.1186/s40463-015-0067-5. PubMed PMID: 25964051; PubMed Central PMCID: PMC4464238.

Takeda M, Kasai T, Morita K, Takeuchi M, Nishikawa T, Yamashita A, et al. Cytopathological features of mammary analogue secretory carcinoma—review of literature. Diagnostic cytopathology. 2015;43(2):131-7. doi: https://doi.org/10.1002/dc.23146. PubMed PMID: 24652816.

1.4.1.5. Epithelial tumour of male breast

1.4.2. Rare epithelial tumours of corpus uteri

1.4.2.1. Squamous cell carcinoma with variants of corpus uteri

1.4.2.2. Adenoid cystic carcinoma of corpus uteri

Zhang M, Pettaway C, Vikram R, Tamboli P. Adenoid cystic carcinoma of the urethra/Cowper's gland with concurrent high-grade prostatic adenocarcinoma: a detailed clinicopathologic case report and review of the literature. Human pathology. 2016;58:138-44. doi: https://doi.org/10.1016/j.humpath.2016.07.027. PubMed PMID: 27554206.

Benhayoune K, El Fatemi H, Bannani A, Melhouf A, Harmouch T. Adenoid cystic carcinoma of cervix: two cases report and review of the literature. The Pan African medical journal. 2015;20:77. doi: https://doi.org/10.11604/pamj.2015.20.77.5720. PubMed PMID: 26090035; PubMed Central PMCID: PMC4450047.

1.4.2.3. Clear cell adenocarcinoma not otherwise specified (NOS) of corpus uteri

Desteli GA, Dogan NU, Gursu T, Ayhan A. Adjuvant therapy for Stage IA uterine clear cell carcinoma with no myometrial invasion: a critical review of literature. European journal of gynaecological oncology. 2016;37(1):17-21. PubMed PMID: 27048103.

Lax SF. [New features in the 2014 WHO classification of uterine neoplasms]. Der Pathologe. 2016;37(6):500-11. doi: https://doi.org/10.1007/s00292-016-0230-4. PubMed PMID: 27738815.

1.4.2.4. Serous (papillary) carcinoma of corpus uteri

Kadour-Peero E, Sagi-Dain L, Cohen G, Korobochka R, Agbarya A, Bejar J, et al. Primary Papillary Serous Carcinoma of the Fallopian Tube Presenting as a Vaginal Mass: A Case Report and Review of the Literature. The American journal of case reports. 2018;19:534-9. doi: https://doi.org/10.12659/AJCR.907444. PubMed PMID: 29731507; PubMed Central PMCID: PMC5967291.

Gao J, Zhang J, Tian W, Teng F, Zhang H, Zhang X, et al. Endometrial cancer with congenital uterine anomalies: 3 case reports and a literature review. Cancer biology & therapy. 2017;18(3):123-31. doi: https://doi.org/10.1080/15384047.2017.1281495. PubMed PMID: 28118070; PubMed Central PMCID: PMC5389419.

Desteli GA, Dogan NU, Gursu T, Ayhan A. Adjuvant therapy for Stage IA uterine clear cell carcinoma with no myometrial invasion: a critical review of literature. European journal of gynaecological oncology. 2016;37(1):17-21. PubMed PMID: 27048103.

Hanley KZ, Fadare O, Fisher KE, Atkins KA, Mosunjac MB. Clinical Significance of Positive Pelvic Washings in Uterine Papillary Serous Carcinoma Confined to an Endometrial Polyp. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2016;35(3):249-55. doi: https://doi.org/10.1097/PGP.0000000000000235. PubMed PMID: 26535985.

Lax SF. [New features in the 2014 WHO classification of uterine neoplasms]. Der Pathologe. 2016;37(6):500-11. doi: https://doi.org/10.1007/s00292-016-0230-4. PubMed PMID: 27738815.

1.4.2.5. Mullerian mixed tumour of corpus uteri

Semczuk A, Ignatov A, Obrzut B, Reventos J, Rechberger T. Role of p53 pathway alterations in uterine carcinosarcomas (malignant mixed Mullerian tumors). Oncology. 2014;87(4):193-204. doi: https://doi.org/10.1159/000363574. PubMed PMID: 25033979.

1.4.3. Epithelial tumours of cervix uteri

1.4.3.1. Squamous cell carcinoma with variants of cervix uteri

Hata M, Koike I, Miyagi E, Numazaki R, Asai-Sato M, Kasuya T, et al. Radiation Therapy for Very Elderly Patients Aged 80 Years and Older With Squamous Cell Carcinoma of the Uterine Cervix. American journal of clinical oncology. 2017;40(2):178-82. doi: https://doi.org/10.1097/COC.0000000000000125. PubMed PMID: 25222073.

Skenderi F, Chikha A, Ibisevic N, Tatarevic-Suko A, Kantardzic N, Vranic S. Skeletal Muscle Metastases from Squamous Cell Carcinoma of the Cervix: Report of Two Cases With Literature Review. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2017;36(1):95-100. doi: https://doi.org/10.1097/PGP.0000000000000298. PubMed PMID: 27391272.

Malpica A. How to approach the many faces of endometrioid carcinoma. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2016;29 Suppl 1:S29-44. doi: https://doi.org/10.1038/modpathol.2015.142. PubMed PMID: 26715172.

Sopracordevole F, Di Giuseppe J, Cervo S, Buttignol M, Giorda G, Ciavattini A, et al. Conservative treatment of coexisting microinvasive squamous and adenocarcinoma of the cervix: report of two cases and literature review. OncoTargets and therapy. 2016;9:539-44. doi: https://doi.org/10.2147/OTT.S93899. PubMed PMID: 26869798; PubMed Central PMCID: PMC4734811.

Turker LB, Gressel GM, Abadi M, Frimer M. Papillary squamous cell carcinoma of the cervix: Two cases and a review of the literature. Gynecologic oncology reports. 2016;18:18-21. doi: https://doi.org/10.1016/j.gore.2016.10.003. PubMed PMID: 27790636; PubMed Central PMCID: PMC5072143.

1.4.3.2. Adenocarcinoma with variants of cervix uteri

Matias-Guiu X, Stewart CJR. Endometriosis-associated ovarian neoplasia. Pathology. 2018;50(2):190-204. doi: https://doi.org/10.1016/j.pathol.2017.10.006. PubMed PMID: 29241974.

Horn LC, Mayr D, Brambs CE, Einenkel J, Sandig I, Schierle K. [Grading of gynecological tumors : Current aspects]. Der Pathologe. 2016;37(4):337-51. doi: https://doi.org/10.1007/s00292-016-0183-7. PubMed PMID: 27379622.

Sopracordevole F, Di Giuseppe J, Cervo S, Buttignol M, Giorda G, Ciavattini A, et al. Conservative treatment of coexisting microinvasive squamous and adenocarcinoma of the cervix: report of two cases and literature review. OncoTargets and therapy. 2016;9:539-44. doi: https://doi.org/10.2147/OTT.S93899. PubMed PMID: 26869798; PubMed Central PMCID: PMC4734811.

Fujiwara H, Yokota H, Monk B, Treilleux I, Devouassoux-Shisheboran M, Davis A, et al. Gynecologic Cancer InterGroup (GCIG) consensus review for cervical adenocarcinoma. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2014;24(9 Suppl 3):S96-101. doi: https://doi.org/10.1097/IGC.0000000000000263. PubMed PMID: 25341589.

Fujiwara K, Monk B, Devouassoux-Shisheboran M. Adenocarcinoma of the uterine cervix: why is it different? Current oncology reports. 2014;16(12):416. doi: https://doi.org/10.1007/s11912-014-0416-y. PubMed PMID: 25325935.

1.4.3.3. Undifferentiated carcinoma of cervix uteri

1.4.3.4. Mullerian mixed tumour of cervix uteri

Al Harbi TZ, Azzam KA, Azzam A, Amin T, Bakshi N. Incidentally Discovered Persistent Mullerian Duct Syndrome in a 45-year-old male presenting with germ cell tumor and bilateral cryptorchidism: A rare case report and review of the literature. International journal of surgery case reports. 2018;43:41-4. doi: https://doi.org/10.1016/j.ijscr.2018.02.002. PubMed PMID: 29453163; PubMed Central PMCID: PMC5849814

1.4.4. Epithelial tumours of ovary and falloppian tube

1.4.4.1. Adenocarcinoma with variants of ovary

Bacalbasa N, Balescu I, Balalau C, Ionescu O, Stoica C. Normal Size Ovary Carcinoma Syndrome with Inguinal Ovarian Cancer Lymph Node Metastases - A Case Report and Literature Review. In vivo. 2018;32(2):385-9. doi: https://doi.org/10.21873/invivo.11250. PubMed PMID: 29475925; PubMed Central PMCID: PMC5905210.

Ge HJ, Bi R, Cheng YF, Chang B, Yu L, Tang SX, et al. [Clinicopathologic analysis of primary carcinoid of the ovary]. Zhonghua bing li xue za zhi = Chinese journal of pathology. 2018;47(7):517-21. doi: https://doi.org/10.3760/cma.j.issn.0529-5807.2018.07.007. PubMed PMID: 29996316.

Mehmood S, Khan MQ. Mucinous Adenocarcinoma Ovary: Diagnostic Dilemma and the Usefulness of Colonoscopy. Journal of Ayub Medical College, Abbottabad : JAMC. 2015;27(2):280-3. PubMed PMID: 26411097.

Suzuki K, Takakura S, Saito M, Morikawa A, Suzuki J, Takahashi K, et al. Impact of surgical staging in stage I clear cell adenocarcinoma of the ovary. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2014;24(7):1181-9. doi: https://doi.org/10.1097/IGC.0000000000000178. PubMed PMID: 25010038.

1.4.4.2. Mucinous adenocarcinoma of ovary

Garg K, Karnezis AN, Rabban JT. Uncommon hereditary gynaecological tumour syndromes: pathological features in tumours that may predict risk for a germline mutation. Pathology. 2018;50(2):238-56. Epub 2018/01/27. doi: https://doi.org/10.1016/j.pathol.2017.10.009. PubMed PMID: 29373116.

Kubecek O, Laco J. The pathogenesis, diagnosis, and management of metastatic tumors to the ovary: a comprehensive review. 2017;34(5):295-307. doi: https://doi.org/10.1007/s10585-017-9856-8. PubMed PMID: 28730323.

Clark ME, Will MD. Intestinal-Type Adenocarcinoma Arising in a Mature Cystic Teratoma of the Ovary. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2016;35(4):352-6. Epub 2016/03/05. doi: https://doi.org/10.1097/pgp.0000000000000258. PubMed PMID: 26937866.

Kurman RJ, Shih Ie M. The Dualistic Model of Ovarian Carcinogenesis: Revisited, Revised, and Expanded. The American journal of pathology. 2016;186(4):733-47. Epub 2016/03/26. doi: https://doi.org/10.1016/j.ajpath.2015.11.011. PubMed PMID: 27012190; PubMed Central PMCID: PMCPmc5808151.

Laurent PE, Thomassin-Piana J, Jalaguier-Coudray A. Mucin-producing tumors of the ovary: MR imaging appearance. Diagnostic and interventional imaging. 2015;96(11):1125-32. Epub 2015/03/11. doi: https://doi.org/10.1016/j.diii.2014.11.034. PubMed PMID: 25753545.

1.4.4.3. Clear cell adenocarcinoma of ovary

Garg K, Karnezis AN, Rabban JT. Uncommon hereditary gynaecological tumour syndromes: pathological features in tumours that may predict risk for a germline mutation. Pathology. 2018;50(2):238-56. Epub 2018/01/27. doi: https://doi.org/10.1016/j.pathol.2017.10.009. PubMed PMID: 29373116.

Matias-Guiu X, Stewart CJR. Endometriosis-associated ovarian neoplasia. Pathology. 2018;50(2):190-204. Epub 2017/12/16. doi: https://doi.org/10.1016/j.pathol.2017.10.006. PubMed PMID: 29241974.

Anglesio MS, Yong PJ. Endometriosis-associated Ovarian Cancers. Clinical obstetrics and gynecology. 2017;60(4):711-27. Epub 2017/10/11. doi: https://doi.org/10.1097/grf.0000000000000320. PubMed PMID: 28990985.

Jang JYA, Yanaihara N. Update on rare epithelial ovarian cancers: based on the Rare Ovarian Tumors Young Investigator Conference. 2017;28(4):e54. doi: https://doi.org/10.3802/jgo.2017.28.e54. PubMed PMID: 28541641.

Plaza-Parrochia F, Romero C, Valladares L, Vega M. Endometrium and steroids, a pathologic overview. Steroids. 2017;126:85-91. Epub 2017/08/23. doi: https://doi.org/10.1016/j.steroids.2017.08.007. PubMed PMID: 28827068.

1.4.4.4. Primary peritoneal serous/papillary carcinoma of ovary

Warembourg S, Cayrac M, Rathat G, Rafii A. Recto-vaginal septum cystadenocarcinoma: a case report and review of the literature. BMC women's health. 2016;16:21. Epub 2016/05/05. doi: https://doi.org/10.1186/s12905-016-0300-z. PubMed PMID: 27142415; PubMed Central PMCID: PMCPmc4855721.

McCluggage WG, Judge MJ, Clarke BA, Davidson B, Gilks CB, Hollema H, et al. Data set for reporting of ovary, fallopian tube and primary peritoneal carcinoma: recommendations from the International Collaboration on Cancer Reporting (ICCR). Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2015;28(8):1101-22. Epub 2015/06/20. doi: https://doi.org/10.1038/modpathol.2015.77. PubMed PMID: 26089092.

Prat J. Ovarian, fallopian tube and peritoneal cancer staging: Rationale and explanation of new FIGO staging 2013. Best practice & research Clinical obstetrics & gynaecology. 2015;29(6):858-69. Epub 2015/04/22. doi: https://doi.org/10.1016/j.bpobgyn.2015.03.006. PubMed PMID: 25890882.

Rai S, Maheshwari A. Management of Fallopian Tube Cancer. Reviews on recent clinical trials. 2015;10(4):276-81. Epub 2015/09/29. PubMed PMID: 26411954.

Singh N, Gilks CB, Wilkinson N, McCluggage WG. Assignment of primary site in high-grade serous tubal, ovarian and peritoneal carcinoma: a proposal. Histopathology. 2014;65(2):149-54. Epub 2014/03/26. doi: https://doi.org/10.1111/his.12419. PubMed PMID: 24660659.

1.4.4.5. Mullerian mixed tumour of ovary

Wheal A, Jenkins R, Mikami Y, Das N, Hirschowitz L. Primary Mucinous Carcinoma of the Fallopian Tube: Case Report and Review of Literature. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2017;36(4):393-9. Epub 2016/09/24. doi: https://doi.org/10.1097/pgp.0000000000000330. PubMed PMID: 27662036.

Kurman RJ, Shih Ie M. Seromucinous Tumors of the Ovary. What's in a Name? International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists.

2016;35(1):78-81. Epub 2015/11/26. doi: https://doi.org/10.1097/pgp.0000000000000266. PubMed PMID: 26598986; PubMed Central PMCID: PMCPmc5512580.

1.4.4.6. Adenocarcinoma with variant of falloppian tube

1.4.5. Non epithelial tumours of ovary

1.4.5.1. Sex cord tumours of ovary

Young RH. Ovarian sex cord-stromal tumours and their mimics. Pathology. 2018;50(1):5-15. Epub 2017/11/15. doi: https://doi.org/10.1016/j.pathol.2017.09.007. PubMed PMID: 29132723.

Boussios S, Moschetta M, Zarkavelis G, Papadaki A, Kefas A, Tatsi K. Ovarian sex-cord stromal tumours and small cell tumours: Pathological, genetic and management aspects. Critical reviews in oncology/hematology. 2017;120:43-51. Epub 2017/12/05. doi: https://doi.org/10.1016/j.critrevonc.2017.10.007. PubMed PMID: 29198337.

Fuller PJ, Leung D, Chu S. Genetics and genomics of ovarian sex cord-stromal tumors. Clinical genetics. 2017;91(2):285-91. Epub 2016/11/05. doi: https://doi.org/10.1111/cge.12917. PubMed PMID: 27813081.

Roth LM, Lyu B, Cheng L. Perspectives on testicular sex cord-stromal tumors and those composed of both germ cells and sex cord-stromal derivatives with a comparison to corresponding ovarian neoplasms. Human pathology. 2017;65:1-14. Epub 2017/04/27. doi: https://doi.org/10.1016/j.humpath.2017.04.009. PubMed PMID: 28445692.

Pang S, Zhang L, Shi Y, Liu Y. Unclassified mixed germ cell-sex cord-stromal tumor with multiple malignant cellular elements in a young woman: a case report and review of the literature. International journal of clinical and experimental pathology. 2014;7(8):5259-66. Epub 2014/09/10. PubMed PMID: 25197407; PubMed Central PMCID: PMCPmc4152097.

1.4.5.2. Malignant/immature teratomas of ovary

Zhang XL, Xu G, Li JL, Pan SH, Yan JJ. Renal immature teratoma in a male adult: A case report and literature review. Medicine. 2018;97(35):e12143. Epub 2018/09/02. doi: https://doi.org/10.1097/md.0000000000012143. PubMed PMID: 30170453.

Wang WC, Lai YC. Evidence of metachronous development of ovarian teratomas: a case report of bilateral mature cystic teratomas of the ovaries and systematic literature review. Journal of ovarian research. 2017;10(1):17. Epub 2017/03/16. doi: https://doi.org/10.1186/s13048-017-0313-8. PubMed PMID: 28288660; PubMed Central PMCID: PMCPmc5348818.

Lee KH, Song MJ, Jung IC, Lee YS, Park EK. Autoamputation of an ovarian mature cystic teratoma: a case report and a review of the literature. 2016;14(1):217. doi: https://doi.org/10.1186/s12957-016-0981-7. PubMed PMID: 27535361.

Moulla AA, Magdy N, Francis N, Taube J, Ronnett BM, El-Bahrawy M. Rare Skin Adnexal and Melanocytic Tumors Arising in Ovarian Mature Cystic Teratomas: A Report of 3 Cases and Review of the Literature. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2016;35(5):448-55. Epub 2016/03/15.

Uma Devi K, Purushotham N, Jayashree N. Management of Ovarian Cancer In Younger Women. Reviews on recent clinical trials. 2015;10(4):263-9. Epub 2015/09/29. PubMed PMID: 26411956.

1.4.5.3. Germ cell tumour of ovary

Tosoni A, Balestrini D, Brandes AA. Fertility preservation in women with CNS tumors. Expert review of anticancer therapy. 2017;17(5):439-45. Epub 2017/04/12. doi: https://doi.org/10.1080/14737140.2017.1316195. PubMed PMID: 28395560.

Sahin B, Karabulut A, Akbulut M, Kaleli B, Yorukoglu A. Ectopic prostatic tissue in mature cystic teratoma of the ovary, a case report and review of the literature. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2016;36(4):513-4. Epub 2016/01/14. doi: https://doi.org/10.3109/01443615.2015.1103718. PubMed PMID: 26757698.

Sharma A, Bhardwaj M, Ahuja A. Rare case of primary trabecular carcinoid tumor of the ovary with unusual presentation. Taiwanese journal of obstetrics & gynecology. 2016;55(5):748-50. Epub 2016/10/19. doi: https://doi.org/10.1016/j.tjog.2015.05.008. PubMed PMID: 27751431.

Vernea F, Volodarsky-Perel A. Mature cystic teratoma of ovary with mucinous epithelial neoplasm and malignant mural nodule: a case report and review of the literature. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2015;34(1):25-9. Epub 2014/12/05. doi: https://doi.org/10.1097/pgp.0000000000000110. PubMed PMID: 25473749.

1.4.6. Epithelial tumours of vulva and vagina

1.4.6.1. Squamous cell carcinoma with variants of vulva and vagina

1.4.6.2. Adenocarcinoma with variants of vulva and vagina

1.4.6.3. Paget s disease of vulva and vagina

1.4.6.4.Undifferentiated carcinoma of vulva and vagina

Patibandla JR, Fehniger JE, Levine DA, Jelinic P. Small cell cancers of the female genital tract: Molecular and clinical aspects. Gynecologic oncology. 2018;149(2):420-7. Epub 2018/02/21. doi: https://doi.org/10.1016/j.ygyno.2018.02.004. PubMed PMID: 29458976.

Howitt BE, Kelly P, McCluggage WG. Pathology of Neuroendocrine Tumours of the Female Genital Tract. Current oncology reports. 2017;19(9):59. Epub 2017/07/25. doi: https://doi.org/10.1007/s11912-017-0617-2. PubMed PMID: 28735441.

Bucchi D, Stracci F, Buonora N, Masanotti G. Human papillomavirus and gastrointestinal cancer: A review. World journal of gastroenterology. 2016;22(33):7415-30. Epub 2016/09/28. doi: https://doi.org/10.3748/wjg.v22.i33.7415. PubMed PMID: 27672265; PubMed Central PMCID: PMCPmc5011658.

de Witte CJ, van de Sande AJ, van Beekhuizen HJ, Koeneman MM, Kruse AJ, Gerestein CG. Imiquimod in cervical, vaginal and vulvar intraepithelial neoplasia: a review. Gynecologic oncology. 2015;139(2):377-84. Epub 2015/09/04. doi: https://doi.org/10.1016/j.ygyno.2015.08.018. PubMed PMID: 26335596.

Rajaram S, Maheshwari A, Srivastava A. Staging for vaginal cancer. Best practice & research Clinical obstetrics & gynaecology. 2015;29(6):822-32. Epub 2015/04/08. doi: https://doi.org/10.1016/j.bpobgyn.2015.01.006. PubMed PMID: 25847318.

1.4.7. Trophoblastic tumour of placenta

Moein-Vaziri N, Fallahi J, Namavar-Jahromi B, Fardaei M, Momtahan M, Anvar Z. Clinical and genetic-epignetic aspects of recurrent hydatidiform mole: A review of literature. Taiwanese journal of obstetrics & gynecology. 2018;57(1):1-6. Epub 2018/02/21. doi: https://doi.org/10.1016/j.tjog.2017.12.001. PubMed PMID: 29458875.

She Q, Cheng Z, El-Chaar D, Luo F, Guo X, Wen SW. Intraplacental choriocarcinoma coexisting with fetomaternal hemorrhage: Case report, chemotherapy management, and literature review. Medicine. 2018;97(14):e9977. Epub 2018/04/06. doi: https://doi.org/10.1097/md.0000000000009977. PubMed PMID: 29620671; PubMed Central PMCID: PMCPmc5902268.

Piechowski J. Trophoblastic-like transdifferentiation: A key to oncogenesis. Critical reviews in oncology/hematology. 2016;101:1-11. Epub 2016/03/08. doi: https://doi.org/10.1016/j.critrevonc.2016.01.019. PubMed PMID: 26948538.

Soygur B, Sati L. The role of syncytins in human reproduction and reproductive organ cancers. Reproduction (Cambridge, England). 2016;152(5):R167-78. Epub 2016/08/04. doi: https://doi.org/10.1530/rep-16-0031. PubMed PMID: 27486264.

Rohilla M, Singh P, Kaur J, Jain V, Gupta N, Prasad GR. Individualistic approach to the management of complete hydatidiform mole with coexisting live fetus. European journal of obstetrics, gynecology, and reproductive biology. 2015;191:39-42. Epub 2015/06/13. doi: https://doi.org/10.1016/j.ejogrb.2015.05.017. PubMed PMID: 26070126.

1.5. Neuroendocrine tumours

1.5.1. Rare neuroendocrine tumours

1.5.1.1. GEP - well differentiated not functing endocrine carcinoma of pancreas and digestive system

Parbhu SK, Adler DG. Pancreatic neuroendocrine tumors: contemporary diagnosis and management. Hospital practice. 2016;44(3):109-19. doi: https://doi.org/10.1080/21548331.2016.1210474. PubMed PMID: 27404266.

Strosberg J, Goldman J, Costa F, Pavel M. The Role of Chemotherapy in Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors. Frontiers of hormone research. 2015;44:239-47. doi: https://doi.org/10.1159/000403785. PubMed PMID: 26303716.

Strosberg JR, Fisher GA, Benson AB, Anthony LB, Arslan B, Gibbs JF, et al. Appropriateness of systemic treatments in unresectable metastatic well-differentiated pancreatic neuroendocrine tumors. World journal of gastroenterology. 2015;21(8):2450-9. doi: https://doi.org/10.3748/wjg.v21.i8.2450. PubMed PMID: 25741154; PubMed Central PMCID: PMC4342923.

Tanaka H, Matsusaki S, Baba Y, Isono Y, Kumazawa H, Sase T, et al. Neuroendocrine tumor G3: a pancreatic well-differentiated neuroendocrine tumor with a high proliferative rate. Clinical journal of gastroenterology. 2015;8(6):414-20. doi: https://doi.org/10.1007/s12328-015-0609-4. PubMed PMID: 26439620.

Yan SX, Adair CF, Balani J, Mansour JC, Gokaslan ST. Solid pseudopapillary neoplasm collides with a well-differentiated pancreatic endocrine neoplasm in an adult man: case report and review of histogenesis. American journal of clinical pathology. 2015;143(2):283-7. doi: https://doi.org/10.1309/AJCP75RYRMWKNQVE. PubMed PMID: 25596255.

1.5.1.2. GEP - well differentiated functing endocrine carcinoma of pancreas and digestive system

Roquin G, Baudin E, Lombard-Bohas C, Cadiot G, Dominguez S, Guimbaud R, et al. Chemotherapy for Well-Differentiated Pancreatic Neuroendocrine Tumours with a Ki-67 Index >/=10%: Is There a More Effective Antitumour Regimen? A Retrospective Multicentre Study of the French Group of Endocrine Tumours (GTE). Neuroendocrinology. 2018;106(1):38-46. doi: https://doi.org/10.1159/000457955. PubMed PMID: 28152531.

Pasricha G, Padhi P, Daboul N, Monga DK. Management of Well-differentiated Gastroenteropancreatic Neuroendocrine Tumors (GEPNETs): A Review. Clinical therapeutics. 2017;39(11):2146-57. doi: https://doi.org/10.1016/j.clinthera.2017.10.010. PubMed PMID: 29173655.

Strosberg JR, Fisher GA, Benson AB, Anthony LB, Arslan B, Gibbs JF, et al. Appropriateness of systemic treatments in unresectable metastatic well-differentiated pancreatic neuroendocrine tumors. World journal of gastroenterology. 2015;21(8):2450-9. doi: https://doi.org/10.3748/wjg.v21.i8.2450. PubMed PMID: 25741154; PubMed Central PMCID: PMC4342923.

Tanaka H, Matsusaki S, Baba Y, Isono Y, Kumazawa H, Sase T, et al. Neuroendocrine tumor G3: a pancreatic well-differentiated neuroendocrine tumor with a high proliferative rate. Clinical journal of gastroenterology. 2015;8(6):414-20. doi: https://doi.org/10.1007/s12328-015-0609-4. PubMed PMID: 26439620.

Yan SX, Adair CF, Balani J, Mansour JC, Gokaslan ST. Solid pseudopapillary neoplasm collides with a well-differentiated pancreatic endocrine neoplasm in an adult man: case report and review of histogenesis. American journal of clinical pathology. 2015;143(2):283-7. doi: https://doi.org/10.1309/AJCP75RYRMWKNQVE. PubMed PMID: 25596255.

1.5.1.3. GEP - poorly differentiated endocrine carcinoma of pancreas and digestive system

Rickman DS, Beltran H, Demichelis F, Rubin MA. Biology and evolution of poorly differentiated neuroendocrine tumors. Nature medicine. 2017;23(6):1-10. doi: https://doi.org/10.1038/nm.4341. PubMed PMID: 28586335.

Walter T, Tougeron D, Baudin E, Le Malicot K, Lecomte T, Malka D, et al. Poorly differentiated gastro-entero-pancreatic neuroendocrine carcinomas: Are they really heterogeneous? Insights from the FFCD-GTE national cohort. European journal of cancer. 2017;79:158-65. doi: https://doi.org/10.1016/j.ejca.2017.04.009. PubMed PMID: 28501762.

Ueda K, Taira T, Hakoda H, Nakata S, Okata S, Nagai T, et al. Giant insulinoma: report of a case and review of published reports. Surgical case reports. 2016;2(1):136. doi: https://doi.org/10.1186/s40792-016-0265-z. PubMed PMID: 27864816; PubMed Central PMCID: PMC5116022.

Sadanandam A, Wullschleger S, Lyssiotis CA, Grotzinger C, Barbi S, Bersani S, et al. A Cross-Species Analysis in Pancreatic Neuroendocrine Tumors Reveals Molecular Subtypes with Distinctive Clinical, Metastatic, Developmental, and Metabolic Characteristics. Cancer discovery. 2015;5(12):1296-313. doi: https://doi.org/10.1158/2159-8290.CD-15-0068. PubMed PMID: 26446169; PubMed Central PMCID: PMC4946251.

Reid MD, Balci S, Saka B, Adsay NV. Neuroendocrine tumors of the pancreas: current concepts and controversies. Endocrine pathology. 2014;25(1):65-79. doi: https://doi.org/10.1007/s12022-013-9295-2. PubMed PMID: 24430597.

1.5.1.4. GEP - mixed endocrine-exocrine carcinoma of pancreas and digestive system

de Mestier L, Cros J, Neuzillet C, Hentic O, Egal A, Muller N, et al. Digestive System Mixed Neuroendocrine-Non-Neuroendocrine Neoplasms. Neuroendocrinology. 2017;105(4):412-25. doi: https://doi.org/10.1159/000475527. PubMed PMID: 28803232.

Serafini S, Da Dalt G, Pozza G, Blandamura S, Valmasoni M, Merigliano S, et al. Collision of ductal adenocarcinoma and neuroendocrine tumor of the pancreas: a case report and review of the literature. World journal of surgical oncology. 2017;15(1):93. doi: https://doi.org/10.1186/s12957-017-1157-9. PubMed PMID: 28464920.

Cazzo E, de Saito HP. Mixed adenoneuroendocrine carcinoma of the gastric stump following Billroth II gastrectomy: case report and review of the literature. Sao Paulo medical journal = Revista paulista de medicina. 2016;134(1):84-7. doi: https://doi.org/10.1590/1516-3180.2013.9080911. PubMed PMID: 25885489.

La Rosa S, Sessa F, Uccella S. Mixed Neuroendocrine-Nonneuroendocrine Neoplasms (MiNENs): Unifying the Concept of a Heterogeneous Group of Neoplasms. Endocrine pathology. 2016;27(4):284-311. doi: https://doi.org/10.1007/s12022-016-9432-9. PubMed PMID: 27169712.

Huang Z, Xiao WD, Li Y, Huang S, Cai J, Ao J. Mixed adenoneuroendocrine carcinoma of the ampulla: two case reports. World journal of gastroenterology. 2015;21(7):2254-9. doi: https://doi.org/10.3748/wjg.v21.i7.2254. PubMed PMID: 25717267; PubMed Central PMCID: PMC4326169.

1.5.1.5. Endocrine carcinoma of thyroid gland

Tavares C, Melo M, Cameselle-Teijeiro JM, Soares P, Sobrinho-Simoes M. ENDOCRINE TUMOURS: Genetic predictors of thyroid cancer outcome. European journal of endocrinology. 2016;174(4):R117-26. doi: https://doi.org/10.1530/EJE-15-0605. PubMed PMID: 26510840.

Trimboli P, Guidobaldi L, Bongiovanni M, Crescenzi A, Alevizaki M, Giovanella L. Use of fine-needle aspirate calcitonin to detect medullary thyroid carcinoma: A systematic review. Diagnostic cytopathology. 2016;44(1):45-51. doi: https://doi.org/10.1002/dc.23375. PubMed PMID: 26481456.

Valderrabano P, Klippenstein DL, Tourtelot JB, Ma Z, Thompson ZJ, Lilienfeld HS, et al. New American Thyroid Association Sonographic Patterns for Thyroid Nodules Perform Well in Medullary Thyroid Carcinoma: Institutional Experience, Systematic Review, and Meta-Analysis. Thyroid : official journal of the American Thyroid Association. 2016;26(8):1093-100. doi: https://doi.org/10.1089/thy.2016.0196. PubMed PMID: 27267210.

Zhang M, Lin O. Molecular Testing of Thyroid Nodules: A Review of Current Available Tests for Fine-Needle Aspiration Specimens. Archives of pathology & laboratory medicine. 2016;140(12):1338-44. doi: https://doi.org/10.5858/arpa.2016-0100-RA. PubMed PMID: 27557410.

Tufano RP, Noureldine SI, Angelos P. Incidental thyroid nodules and thyroid cancer: considerations before determining management. JAMA otolaryngology—head & neck surgery. 2015;141(6):566-72. doi: https://doi.org/10.1001/jamaoto.2015.0647. PubMed PMID: 25928353.

1.5.1.6. Rare neuroendocrine carcinoma of skin

Tello TL, Coggshall K, Yom SS, Yu SS. Merkel cell carcinoma: An update and review: Current and future therapy. Journal of the American Academy of Dermatology. 2018;78(3):445-54. doi: https://doi.org/10.1016/j.jaad.2017.12.004. PubMed PMID: 29229573.

van Veenendaal LM, van Akkooi ACJ, Verhoef C, Grunhagen DJ, Klop WMC, Valk GD, et al. Merkel cell carcinoma: Clinical outcome and prognostic factors in 351 patients. Journal of surgical oncology. 2018. doi: https://doi.org/10.1002/jso.25090. PubMed PMID: 29790179.

Zanetti I, Coati I, Alaibac M. Interaction between Merkel cell carcinoma and the immune system: Pathogenetic and therapeutic implications. Molecular and clinical oncology. 2017;7(5):729-32. doi: https://doi.org/10.3892/mco.2017.1406. PubMed PMID: 29142746; PubMed Central PMCID: PMC5666639.

Thar YY, Patel P, Huang T, Guevara E. An Extremely Rare Case of Advanced Metastatic Small Cell Neuroendocrine Carcinoma of Sinonasal Tract. Case reports in oncological medicine. 2016;2016:1496916. doi: https://doi.org/10.1155/2016/1496916. PubMed PMID: 27529044; PubMed Central PMCID: PMC4978830.

Westerveld DR, Hall DJ, Richards WT. Merkel Cell Carcinoma of the Hand: A Case Report and Review of the Literature. Hand. 2016;11(4):NP24-NP9. doi: https://doi.org/10.1177/1558944715616098. PubMed PMID: 28149222; PubMed Central PMCID: PMC5256641.

1.5.1.7. Typical and atypical carcinoid of the lung

Zhao J, Shao J, Zhao R, Li R, Yu K, Zhu L, et al. Histological evolution from primary lung adenocarcinoma harboring EGFR mutation to high-grade neuroendocrine carcinoma. Thoracic cancer. 2018;9(1):129-35. doi: https://doi.org/10.1111/1759-7714.12549. PubMed PMID: 29120087; PubMed Central PMCID: PMC5754316.

Zhou F, Hou L, Ding T, Song Q, Chen X, Su C, et al. Distinct clinicopathologic features, genomic characteristics and survival of central and peripheral pulmonary large cell neuroendocrine carcinoma: From different origin cells? Lung cancer. 2018;116:30-7. doi: https://doi.org/10.1016/j.lungcan.2017.12.009. PubMed PMID: 29413048.

Wolin EM. Advances in the Diagnosis and Management of Well-Differentiated and Intermediate-Differentiated Neuroendocrine Tumors of the Lung. Chest. 2017;151(5):1141-6. doi: https://doi.org/10.1016/j.chest.2016.06.018. PubMed PMID: 27373769.

Yang G, Pan Z, Ma N, Qu L, Yuan T, Pang X, et al. Leptomeningeal metastasis of pulmonary large-cell neuroendocrine carcinoma: A case report and review of the literature. Oncology letters. 2017;14(4):4282-6. doi: https://doi.org/10.3892/ol.2017.6676. PubMed PMID: 28943940; PubMed Central PMCID: PMC5605966.

Wick MR, Marchevsky AM. Neuroendocrine neoplasms of the lung: Concepts and terminology. Seminars in diagnostic pathology. 2015;32(6):445-55. doi: https://doi.org/10.1053/j.semdp.2015.09.012. PubMed PMID: 26500079.

1.5.1.8. Rare neuroendocrine carcinoma of other sites

Wang G, Xiao L, Zhang M, Kamat AM, Siefker-Radtke A, Dinney CP, et al. Small cell carcinoma of the urinary bladder: a Clinicopathologic and Immunohistochemical analysis of 81 cases. Human pathology. 2018. doi: https://doi.org/10.1016/j.humpath.2018.05.005. PubMed PMID: 29763719.

Visscher DW, Yasir S. Neuroendocrine Tumors of the Breast. Endocrine pathology. 2017;28(2):121-7. doi: https://doi.org/10.1007/s12022-017-9477-4. PubMed PMID: 28389994.

Yang X, Cao Y, Chen C, Liu L, Wang C, Liu S. Primary neuroendocrine breast carcinomas: a retrospective analysis and review of literature. OncoTargets and therapy. 2017;10:397-407. doi: https://doi.org/10.2147/OTT.S113736. PubMed PMID: 28176908; PubMed Central PMCID: PMC5261841.

Wang X, Li Y, Feng H, Wang C, Chen J, Liu L. Large cell neuroendocrine carcinoma of the ileocecal junction with well differentiation adenocarcinoma. Neuro endocrinology letters. 2015;36(2):133-5. PubMed PMID: 26071581.

Wang J, Wei B, Albarracin CT, Hu J, Abraham SC, Wu Y. Invasive neuroendocrine carcinoma of the breast: a population-based study from the surveillance, epidemiology and end results (SEER) database. BMC cancer. 2014;14:147. doi: https://doi.org/10.1186/1471-2407-14-147. PubMed PMID: 24589259; PubMed Central PMCID: PMC3974013.

1.5.1.9. Pheochromocytoma malignant

Turchini J, Cheung VKY, Tischler AS, De Krijger RR, Gill AJ. Pathology and genetics of phaeochromocytoma and paraganglioma. Histopathology. 2018;72(1):97-105. doi: https://doi.org/10.1111/his.13402. PubMed PMID: 29239044.

Wang H, Zhang S, Zhang A, Yan C. Propofol Prevents the Progression of Malignant Pheochromocytoma In Vitro and In Vivo. DNA and cell biology. 2018;37(4):308-15. doi: https://doi.org/10.1089/dna.2017.3972. PubMed PMID: 29565198.

Uysal E, Kirdak T, Gurer AO, Ikidag MA. Giant multicystic malignant pheochromocytoma. Turkish journal of surgery. 2017;33(4):296-8. doi: https://doi.org/10.5152/UCD.2015.3011. PubMed PMID: 29260138; PubMed Central PMCID: PMC5731569.

Yu R. Proteasome Inhibitors: A Potential Medical Therapy for Malignant Pheochromocytoma. Endocrinology. 2017;158(10):3083-5. doi: https://doi.org/10.1210/en.2017-00742. PubMed PMID: 28977615.

Toledo RA, Dahia PL. Next-generation sequencing for the diagnosis of hereditary pheochromocytoma and paraganglioma syndromes. Current opinion in endocrinology, diabetes, and obesity. 2015;22(3):169-79. doi: https://doi.org/10.1097/MED.0000000000000150. PubMed PMID: 25871962.

1.5.1.10. Paraganglioma

Yuan M, Xu C, Yang G, Wang W. Pediatric paraganglioma of the posterior mediastinum: A case report and review of literature. Medicine. 2018;97(27):e11212. doi: https://doi.org/10.1097/MD.0000000000011212. PubMed PMID: 29979384; PubMed Central PMCID: PMC6076022.

Yi C, Han L, Yang R, Yu J. Paraganglioma of the renal pelvis: a case report and review of literature. Tumori. 2017;103(Suppl. 1):e47-e9. doi: https://doi.org/10.5301/tj.5000677. PubMed PMID: 28799639.

Zeng J, Simsir A, Oweity T, Hajdu C, Cohen S, Shi Y. Peripancreatic paraganglioma mimics pancreatic/gastrointestinal neuroendocrine tumor on fine needle aspiration: Report of two cases and review of the literature. Diagnostic cytopathology. 2017;45(10):947-52. doi: https://doi.org/10.1002/dc.23761. PubMed PMID: 28560856.

Zhikrivetskaya SO, Snezhkina AV, Zaretsky AR, Alekseev BY, Pokrovsky AV, Golovyuk AL, et al. Molecular markers of paragangliomas/pheochromocytomas. Oncotarget. 2017;8(15):25756-82. doi: https://doi.org/10.18632/oncotarget.15201. PubMed PMID: 28187001; PubMed Central PMCID: PMC5421967.

Zi J, Ma C, Xu C, Bai Y. A pediatric malignant paraganglioma and brief review of the literature. Hellenic journal of nuclear medicine. 2016;19(3):281-4. doi: https://doi.org/10.1967/s002449910413. PubMed PMID: 27824970.

1.6. Tumours of the endocrine organs

1.6.1. Carcinomas of pituitary gland

Yoo F, Kuan EC, Heaney AP, Bergsneider M, Wang MB. Corticotrophic pituitary carcinoma with cervical metastases: case series and literature review. Pituitary. 2018;21(3):290-301. doi: https://doi.org/10.1007/s11102-018-0872-8. PubMed PMID: 29404894.

Zhao Y, Zhang H, Lian W, Xing B, Feng M, Liu X, et al. Collision tumors composed of meningioma and growth hormone-secreting pituitary adenoma in the sellar region: Case reports and a literature review. Medicine. 2017;96(50):e9139. doi: https://doi.org/10.1097/MD.0000000000009139. PubMed PMID: 29390316; PubMed Central PMCID: PMCPMC5815728.

Yang Z, Zhang T, Gao H. Genetic aspects of pituitary carcinoma: A systematic review. Medicine. 2016;95(47):e5268. doi: https://doi.org/10.1097/MD.0000000000005268. PubMed PMID: 27893664; PubMed Central PMCID: PMCPMC5134857.

Zhan X, Wang X, Cheng T. Human Pituitary Adenoma Proteomics: New Progresses and Perspectives. Front Endocrinol (Lausanne). 2016;7:54. doi: https://doi.org/10.3389/fendo.2016.00054. PubMed PMID: 27303365; PubMed Central PMCID: PMCPMC4885873.

Xu K, Yuan Y, Zhou J, Yu J. Pituitary adenoma apoplexy caused by rupture of an anterior communicating artery aneurysm: case report and literature review. World J Surg Oncol. 2015;13:228. doi:

https://doi.org/10.1186/s12957-015-0653-z. PubMed PMID: 26220796; PubMed Central PMCID: PMCPMC4518590.

1.6.2. Carcinomas of thyroid gland

Tiedje V, Stuschke M, Weber F, Dralle H, Moss L, Fuhrer D. Anaplastic thyroid carcinoma: review of treatment protocols. Endocrine-related cancer. 2018;25(3):R153-R61. doi: https://doi.org/10.1530/ERC-17-0435. PubMed PMID: 29295821.

Vuong HG, Odate T, Duong UNP, Mochizuki K, Nakazawa T, Katoh R, et al. Prognostic importance of solid variant papillary thyroid carcinoma: A systematic review and meta-analysis. Head Neck. 2018;40(7):1588-97. doi: https://doi.org/10.1002/hed.25123. PubMed PMID: 29509280.

Zhang Y, Yang J, Zhang M, Meng Z, Song W, Yang L, et al. Thyroid follicular carcinoma-like renal tumor: A case report and literature review. Medicine. 2018;97(21):e10815. doi: https://doi.org/10.1097/MD.0000000000010815. PubMed PMID: 29794767.

Yapa S, Mulla O, Green V, England J, Greenman J. The Role of Chemokines in Thyroid Carcinoma. Thyroid. 2017;27(11):1347-59. doi: https://doi.org/10.1089/thy.2016.0660. PubMed PMID: 28891394.

Visciano C, Prevete N, Liotti F, Marone G. Tumor-Associated Mast Cells in Thyroid Cancer. Int J Endocrinol. 2015;2015:705169. doi: https://doi.org/10.1155/2015/705169. PubMed PMID: 26379707; PubMed Central PMCID: PMCPMC4563106.

1.6.3. Carcinomas of parathyroid gland

Di Meo G, Sgaramella LI, Ferraro V, Prete FP, Gurrado A, Testini M. Parathyroid carcinoma in multiple endocrine neoplasm type 1 syndrome: case report and systematic literature review. Clin Exp Med. 2018. doi: https://doi.org/10.1007/s10238-018-0512-7. PubMed PMID: 29922966.

Fernandes JMP, Paiva C, Correia R, Polonia J, Moreira da Costa A. Parathyroid carcinoma: From a case report to a review of the literature. Int J Surg Case Rep. 2018;42:214-7. doi: https://doi.org/10.1016/j.ijscr.2017.11.030. PubMed PMID: 29353223; PubMed Central PMCID: PMCPMC5985244.

Goswamy J, Lei M, Simo R. Parathyroid carcinoma. Curr Opin Otolaryngol Head Neck Surg. 2016;24(2):155-62. doi: https://doi.org/10.1097/MOO.0000000000000234. PubMed PMID: 26771263.

Medas F, Erdas E, Loi G, Podda F, Pisano G, Nicolosi A, et al. Controversies in the management of parathyroid carcinoma: A case series and review of the literature. Int J Surg. 2016;28 Suppl 1:S94-8. doi: https://doi.org/10.1016/j.ijsu.2015.12.040. PubMed PMID: 26708847.

Tejera Hernandez AA, Gutierrez Giner MI, Vega Benitez V, Fernandez San Millan D, Hernandez Hernandez JR. Intrathyroidal parathyroid carcinoma. A case report and review of literature. Endocrinol Nutr. 2016;63(1):46-8. doi: https://doi.org/10.1016/j.endonu.2015.09.004. PubMed PMID: 26588997.

1.6.4. Carcinoma of adrenal gland

Toledo R, Jimenez C. Recent advances in the management of malignant pheochromocytoma and paraganglioma: focus on tyrosine kinase and hypoxia-inducible factor inhibitors. F1000Res. 2018;7. doi: https://doi.org/10.12688/f1000research.13995.1. PubMed PMID: 30109021; PubMed Central PMCID: PMCPMC6069727.

Varghese J, Habra MA. Update on adrenocortical carcinoma management and future directions. Curr Opin Endocrinol Diabetes Obes. 2017;24(3):208-14. doi: https://doi.org/10.1097/MED.0000000000000332. PubMed PMID: 28277340.

Toledo RA, Dahia PL. Next-generation sequencing for the diagnosis of hereditary pheochromocytoma and paraganglioma syndromes. Curr Opin Endocrinol Diabetes Obes. 2015;22(3):169-79. doi: https://doi.org/10.1097/MED.0000000000000150. PubMed PMID: 25871962.

Wanis KN, Kanthan R. Diagnostic and prognostic features in adrenocortical carcinoma: a single institution case series and review of the literature. World J Surg Oncol. 2015;13:117. doi: https://doi.org/10.1186/s12957-015-0527-4. PubMed PMID: 25889798; PubMed Central PMCID: PMCPMC4384320.

Woo S, Cho JY, Kim SY, Kim SH. Adrenal adenoma and metastasis from clear cell renal cell carcinoma: can they be differentiated using standard MR techniques? Acta Radiol. 2014;55(9):1120-8. doi: https://doi.org/10.1177/0284185113512301. PubMed PMID: 24252816.

1.7. CNS tumours

1.7.1. Tumours of central nervous system (CNS)

1.7.1.1. Astrocytic tumours of CNS

Stoyanov GS, Dzhenkov D, Ghenev P, Iliev B, Enchev Y, Tonchev AB. Cell biology of glioblastoma multiforme: from basic science to diagnosis and treatment. Medical oncology (Northwood, London, England). 2018;35(3):27. Epub 2018/02/02. doi: https://doi.org/10.1007/s12032-018-1083-x. PubMed PMID: 29387965.

Schittenhelm J. Recent advances in subtyping tumors of the central nervous system using molecular data. Expert review of molecular diagnostics. 2017;17(1):83-94. Epub 2016/11/29. doi: https://doi.org/10.1080/14737159.2017.1266259. PubMed PMID: 27893285.

Gondi V, Yock TI, Mehta MP. Proton therapy for paediatric CNS tumours - improving treatment-related outcomes. Nature reviews Neurology. 2016;12(6):334-45. Epub 2016/05/21. doi: https://doi.org/10.1038/nrneurol.2016.70. PubMed PMID: 27197578.

Hostenbach S, D'Haeseleer M, Kooijman R, De Keyser J. The pathophysiological role of astrocytic endothelin-1. Progress in neurobiology. 2016;144:88-102. Epub 2016/05/03. doi: https://doi.org/10.1016/j.pneurobio.2016.04.009. PubMed PMID: 27132521.

Perry A, Wesseling P. Histologic classification of gliomas. Handbook of clinical neurology. 2016;134:71-95. Epub 2016/03/08. doi: https://doi.org/10.1016/b978-0-12-802997-8.00005-0. PubMed PMID: 26948349.

1.7.1.2. Oligodendroglial tumours of CNS

Komori T. Pathology of oligodendroglia: An overview. Neuropathology : official journal of the Japanese Society of Neuropathology. 2017;37(5):465-74. Epub 2017/05/27. doi: https://doi.org/10.1111/neup.12389. PubMed PMID: 28548216.

Schittenhelm J. Recent advances in subtyping tumors of the central nervous system using molecular data. Expert review of molecular diagnostics. 2017;17(1):83-94. Epub 2016/11/29. doi: https://doi.org/10.1080/14737159.2017.1266259. PubMed PMID: 27893285.

Perry A, Wesseling P. Histologic classification of gliomas. Handbook of clinical neurology. 2016;134:71-95. Epub 2016/03/08. doi: https://doi.org/10.1016/b978-0-12-802997-8.00005-0. PubMed PMID: 26948349.

1.7.1.3. Ependymal tumours of CNS

Leeper H, Felicella MM, Walbert T. Recent Advances in the Classification and Treatment of Ependymomas. Current treatment options in oncology. 2017;18(9):55. Epub 2017/08/11. doi: https://doi.org/10.1007/s11864-017-0496-7. PubMed PMID: 28795287.

Schittenhelm J. Recent advances in subtyping tumors of the central nervous system using molecular data. Expert review of molecular diagnostics. 2017;17(1):83-94. Epub 2016/11/29. doi: https://doi.org/10.1080/14737159.2017.1266259. PubMed PMID: 27893285.

Gondi V, Yock TI, Mehta MP. Proton therapy for paediatric CNS tumours - improving treatment-related outcomes. Nature reviews Neurology. 2016;12(6):334-45. Epub 2016/05/21. doi: https://doi.org/10.1038/nrneurol.2016.70. PubMed PMID: 27197578.

Perry A, Wesseling P. Histologic classification of gliomas. Handbook of clinical neurology. 2016;134:71-95. Epub 2016/03/08. doi: https://doi.org/10.1016/b978-0-12-802997-8.00005-0. PubMed PMID: 26948349.

Biswas A, Chaudhari PB, M SK, Sigamani E, Sharma MC, Kalra SK, et al. Primary pineal malignant melanoma - illustrated review. Turkish neurosurgery. 2015;25(2):201-9. Epub 2015/05/28. doi: https://doi.org/10.5137/1019-5149.jtn.6568-12.1. PubMed PMID: 26014001.

1.7.1.4 Choroid plexus carcinoma of CNS

Yang M, Chen X, Wang N, Zhu K, Hu YZ, Zhao Y, et al. Primary atypical teratoid/rhabdoid tumor of central nervous system in children: a clinicopathological analysis and review of literature in China. International journal of clinical and experimental pathology. 2014;7(5):2411-20. Epub 2014/06/27. PubMed PMID: 24966951; PubMed Central PMCID: PMCPmc4069879.

1.7.1.5. Malignant meningiomas

Zakhari N, Torres C, Castillo M, Nguyen TB. Uncommon Cranial Meningioma: Key Imaging Features on Conventional and Advanced Imaging. Clinical neuroradiology. 2017;27(2):135-44. Epub 2017/05/04. doi: https://doi.org/10.1007/s00062-017-0583-y. PubMed PMID: 28466126.

Zamanipoor Najafabadi AH, Peeters MCM, Dirven L, Lobatto DJ, Groen JL, Broekman MLD, et al. Impaired health-related quality of life in meningioma patients-a systematic review. Neuro-oncology. 2017;19(7):897-907. Epub 2017/01/01. doi: https://doi.org/10.1093/neuonc/now250. PubMed PMID: 28039363; PubMed Central PMCID: PMCPmc5570251.

Zhao P, Li N, Cao J, Lin X, Liang C. Rhabdoid Meningioma Arising Concurrent in Pulmonary and Intracranial with a Rare Malignant Clinical Progression: Case Report and Literature Review. World neurosurgery. 2017;107:1046.e17-.e22. Epub 2017/08/12. doi: https://doi.org/10.1016/j.wneu.2017.07.181. PubMed PMID: 28797981.

Zhao Y, Zhang H, Lian W, Xing B, Feng M, Liu X, et al. Collision tumors composed of meningioma and growth hormone-secreting pituitary adenoma in the sellar region: Case reports and a literature review. Medicine. 2017;96(50):e9139. Epub 2018/02/03. doi: https://doi.org/10.1097/md.0000000000009139. PubMed PMID: 29390316; PubMed Central PMCID: PMCPmc5815728.

Zhang D, Yu J, Guo Y, Zhao S, Shao G, Huang H. An intraventricular meningioma and recurrent astrocytoma collision tumor: a case report and literature review. World journal of surgical oncology. 2015;13:37. Epub 2015/04/19. doi: https://doi.org/10.1186/s12957-015-0436-6. PubMed PMID: 25889820; PubMed Central PMCID: PMCPmc4329203.

1.7.2. Embryonal tumours of central nervous system (CNS)

Zhang I, Formenti SC, Knisely JPS. Immunotherapy Plus Stereotactic Radiosurgery: Building on the Promise of Precision Medicine for CNS Malignancies-PART 1: Principles of Combined Treatment. Oncology (Williston Park, NY). 2018;32(2):e28-e32. Epub 2018/03/02. PubMed PMID: 29492951.

Yin J, Valin KL, Dixon ML, Leavenworth JW. The Role of Microglia and Macrophages in CNS Homeostasis, Autoimmunity, and Cancer. Journal of immunology research. 2017;2017:5150678. Epub 2018/02/08. doi: https://doi.org/10.1155/2017/5150678. PubMed PMID: 29410971; PubMed Central PMCID: PMCPmc5749282.

Yust Katz S, Cachia D, Kamiya-Matsuoka C, Olar A, Theeler B, Penas Prado M, et al. Ependymomas arising outside of the central nervous system: A case series and literature review. Journal of clinical

neuroscience : official journal of the Neurosurgical Society of Australasia. 2018;47:202-7. Epub 2017/10/22. doi: https://doi.org/10.1016/j.jocn.2017.10.026. PubMed PMID: 29054328.

Yang I, Ung N, Chung LK, Nagasawa DT, Thill K, Park J, et al. Clinical manifestations of central neurocytoma. Neurosurgery clinics of North America. 2015;26(1):5-10. Epub 2014/11/30. doi: https://doi.org/10.1016/j.nec.2014.09.011. PubMed PMID: 25432178.

Yang M, Chen X, Wang N, Zhu K, Hu YZ, Zhao Y, et al. Primary atypical teratoid/rhabdoid tumor of central nervous system in children: a clinicopathological analysis and review of literature in China. International journal of clinical and experimental pathology. 2014;7(5):2411-20. Epub 2014/06/27. PubMed PMID: 24966951; PubMed Central PMCID: PMCPmc4069879.

1.8. Sarcomas

1.8.1. Soft tissue sarcoma

1.8.1.1. Soft tissue sarcoma of head and neck

Wolter NE, Adil E, Irace AL, Werger A, Perez-Atayde AR, Weldon C, et al. Malignant glomus tumors of the head and neck in children and adults: Evaluation and management. The Laryngoscope. 2017;127(12):2873-82. Epub 2017/03/16. doi: https://doi.org/10.1002/lary.26550. PubMed PMID: 28294349.

Zhu W, Hu F, Zhao T, Wang C, Tao Q. Clinical Characteristics of Radiation-Induced Sarcoma of the Head and Neck: Review of 15 Cases and 323 Cases in the Literature. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2016;74(2):283-91. Epub 2015/08/16. doi: https://doi.org/10.1016/j.joms.2015.07.013. PubMed PMID: 26275593.

Wong BL, Lee VN, Tikka T, Kim D, Dwivedi RC. Kaposiform haemangioendothelioma of the head and neck. Critical reviews in oncology/hematology. 2016;104:156-68. Epub 2016/07/02. doi: https://doi.org/10.1016/j.critrevonc.2016.06.005. PubMed PMID: 27365122.

Zhou DN, Yang QQ, Li ZL, Pan ZY, Deng YF. Head and neck rhabdomyosarcoma: follow-up results of four cases and review of the literature. International journal of clinical and experimental pathology. 2015;8(5):4277-83. Epub 2015/07/21. PubMed PMID: 26191120; PubMed Central PMCID: PMCPmc4502992.

Zhang I, Zaorsky NG, Abraham JA, Tuluc M, Curry JM, Bar-Ad V. Chondrosarcoma of the hyoid bone: case report and review of current management options. Head & neck. 2014;36(7):E65-72. Epub 2013/05/31. doi: https://doi.org/10.1002/hed.23373. PubMed PMID: 23720060.

1.8.1.2. Soft tissue sarcoma of limbs

Alshareef MA, Almadidy Z, Baker T, Perry A, Welsh CT, Vandergrift WA, 3rd. Intracranial Angiomatoid Fibrous Histiocytoma: Case Report and Literature Review. World neurosurgery. 2016;96:403-9. Epub 2016/09/27. doi: https://doi.org/10.1016/j.wneu.2016.09.059. PubMed PMID: 27667574.

Divani KG, O'Brien A, Molloy S, Trivedi J, Cowan J, Gibson A. A multicentre retrospective review of muscle necrosis of the leg following spinal surgery with motor evoked potential monitoring: a cause for concern? European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2016;25(3):801-6. Epub 2015/06/13. doi: https://doi.org/10.1007/s00586-015-4063-2. PubMed PMID: 26063055

Au S, Juhl ME, Emmadi R, Krunic AL. Nail dystrophy as a presenting sign of a chondrosarcoma of the distal phalanx - case report and review of the literature. Acta dermato-venereologica. 2015;95(8):1026-7. Epub 2015/04/18. doi: https://doi.org/10.2340/00015555-2118. PubMed PMID: 25881814.

Byerly S, Chopra S, Nassif NA, Chen P, Sener SF, Eisenberg BL, et al. The role of margins in extremity soft tissue sarcoma. Journal of surgical oncology. 2016;113(3):333-8. Epub 2015/12/15. doi: https://doi.org/10.1002/jso.24112. PubMed PMID: 26662660.

Chao AH, Mayerson JL, Chandawarkar R, Scharschmidt TJ. Surgical management of soft tissue sarcomas: extremity sarcomas. Journal of surgical oncology. 2015;111(5):540-5. Epub 2014/10/23. doi: https://doi.org/10.1002/jso.23810. PubMed PMID: 25335973.

1.8.1.3. Soft tissue sarcoma of superficial trunk

Scaglioni MF, Giuseppe AD, Chang EI. Propeller flap reconstruction of abdominal defects: review of the literature and case report. Microsurgery. 2015;35(1):72-8. Epub 2014/04/18. doi: https://doi.org/10.1002/micr.22262. PubMed PMID: 24740891.

Wang HW, Dai W, Qin XJ, Zhang CP. A new clinical manifestation for cheek alveolar soft-part sarcoma: a case report and review of the literature. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2014;72(4):817-22. Epub 2013/12/18. doi: https://doi.org/10.1016/j.joms.2013.10.019. PubMed PMID: 24342574.

1.8.1.4. Soft tissue sarcoma of mediastinum

Jin L, Sui Y, Zhu H, Chen Z, Liu S. Primary mediastinal clear cell sarcoma: a case report and review of the literature. Diagnostic pathology. 2017;12(1):5. Epub 2017/01/15. doi: https://doi.org/10.1186/s13000-016-0594-z. PubMed PMID: 28086809; PubMed Central PMCID: PMCPmc5237244.

Purkait S, Mallick S, Joshi PP, Mallick S, Murugan NV, Sharma MC, et al. Retroperitoneal and mediastinal follicular dendritic cell sarcoma: report of 3 cases with review of literature. Hematological oncology. 2017;35(3):374-9. Epub 2015/12/08. doi: https://doi.org/10.1002/hon.2275. PubMed PMID: 26639109.

Tanaka Y, Hokka D, Ogawa H, Shimizu N, Inoue T, Tanaka H, et al. Surgery for malignant lesions of the chest which extensively involved the mediastinum, lung, and heart. General thoracic and cardiovascular surgery. 2017;65(7):365-73. Epub 2017/05/26. doi: https://doi.org/10.1007/s11748-017-0782-0. PubMed PMID: 28540630.

Ukekwe FI, Ezemba N, Olusina DB, Igbokwe U, Ngene C. Giant primary synovial sarcoma of the anterior mediastinum: A case report and review of literature. Nigerian journal of clinical practice. 2016;19(2):293-7. Epub 2016/02/10. doi: https://doi.org/10.4103/1119-3077.175965. PubMed PMID: 26856298.

Yu H, Wu Z, Cui Y, Huang J. Low-grade extraskeletal osteosarcoma of the mediastinum: report of a case and review of literature. International journal of clinical and experimental pathology. 2015;8(3):3279-81. Epub 2015/06/06. PubMed PMID: 26045852; PubMed Central PMCID: PMCPmc4440161.

1.8.1.5. Soft tissue sarcoma of heart

Sun YP, Wang X, Gao YS, Zhao S, Bai Y. Primary cardiac sarcoma complicated with cerebral infarction and brain metastasis: A case report and literature review. Cancer biomarkers : section A of Disease markers. 2017;21(1):247-50. Epub 2017/11/01. doi: https://doi.org/10.1186/s13019-017-0654-9 PubMed PMID: 29060931.

Burke A, Tavora F. The 2015 WHO Classification of Tumors of the Heart and Pericardium. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2016;11(4):441-52. Epub 2016/01/05. doi: https://doi.org/10.1016/j.jtho.2015.11.009. PubMed PMID: 26725181.

Prifti E, Ademaj F, Ikonomi M, Demiraj A. Unusual localization of a primary pleomorphic malignant fibrous histiocytoma on the mitral valve: a case report and review of the literature. Journal of medical case

reports. 2015;9:246. Epub 2015/11/01. doi: https://doi.org/10.1186/s13256-015-0726-1. PubMed PMID: 26518517; PubMed Central PMCID: PMCPmc4628272.

Goldblatt J, Saxena P, McGiffin DC, Zimmet A. Pericardial Synovial Sarcoma: A Rare Clinical Entity. Journal of cardiac surgery. 2015;30(11):801-4. Epub 2015/09/09. doi: https://doi.org/10.1111/jocs.12609. PubMed PMID: 26347295.

Yoshino M, Sekine Y, Koh E, Kume Y, Saito H, Kimura S, et al. Pericardial synovial sarcoma: a case report and review of the literature. Surgery today. 2014;44(11):2167-73. Epub 2013/09/12. doi: https://doi.org/10.1007/s00595-013-0720-4. PubMed PMID: 24022581.

1.8.1.6. Soft tissue sarcoma of breast

Derman YE. Clinical Practice Recommendations Based on an Updated Review of Breast Cancer Risk Among Women Treated for Childhood Cancer. Journal of pediatric oncology nursing : official journal of the Association of Pediatric Oncology Nurses. 2018;35(1):65-78. Epub 2017/09/03. doi: https://doi.org/10.1177/1043454217727515. PubMed PMID: 28863725.

Duncan MA, Lautner MA. Sarcomas of the Breast. The Surgical clinics of North America. 2018;98(4):869-76. Epub 2018/07/15. doi: https://doi.org/10.1016/j.suc.2018.03.013. PubMed PMID: 30005780.

Bansal A, Kaur M, Dalal V. Pleomorphic Sarcoma of Breast: A Report of Two Cases and Review of Literature. Acta medica Iranica. 2017;55(4):272-6. Epub 2017/05/24. PubMed PMID: 28532141.

Yoshiba S, Saotome T, Mikogami T, Shirota T. Metastasis of Mammary Gland Malignant Phyllodes Tumor to the Mandibular Region: A Case Report and Review of the Literature. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2017;75(2):440.e1-.e9. Epub 2016/10/22. doi:https://doi.org/10.1016/j.joms.2016.09.024. PubMed PMID: 27765548.

Yadav SK, Yadav J, Abhinav A, Satish K, Om P, Manish K, et al. Ulcerated primary fibrosarcoma of breast: case report and review of literature. Breast disease. 2015;35(1):41-4. Epub 2014/08/07. doi: https://doi.org/10.3233/bd-140382. PubMed PMID: 25095986.

1.8.1.7. Soft tissue sarcoma of uterus

Desar IME, Ottevanger PB, Benson C, van der Graaf WTA. Systemic treatment in adult uterine sarcomas. Critical reviews in oncology/hematology. 2018;122:10-20. Epub 2018/02/21. doi: https://doi.org/10.1016/j.critrevonc.2017.12.009. PubMed PMID: 29458779.

Mandato VD, Torricelli F, Mastrofilippo V, Valli R, Aguzzoli L, La Sala GB. Primary extra-uterine and extra-ovarian mullerian adenosarcoma: case report and literature review. BMC cancer. 2018;18(1):134. Epub 2018/02/07. doi: https://doi.org/10.1186/s12885-018-4037-y. PubMed PMID: 29402239; PubMed Central PMCID: PMCPmc5800024.

Modaffari P, D'Alonzo M, Garbagnati M, Pecchio S, Menato G, Biglia N. Unexpected uterine leiomyosarcoma in a woman with multiple myomas treated with ulipristal acetate: case report and literature review. 2018;34(3):192-4. doi: https://doi.org/10.1080/09513590.2017.1380186. PubMed PMID: 28933575.

Tanos V, Berry KE. Benign and malignant pathology of the uterus. Best practice & research Clinical obstetrics & gynaecology. 2018;46:12-30. Epub 2017/11/12. doi: https://doi.org/10.1016/j.bpobgyn.2017.10.004. PubMed PMID: 29126743.

Petca AT, Vladareanu S, Radu DC, Bo TM, Berceanu C, Mastalier Manolescu BS, et al. Morphological, imaging and surgical aspects in a complex case of uterine leiomyosarcoma - case report and review of the literature. Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie. 2017;58(2):619-25. Epub 2017/07/22. PubMed PMID: 28730252.

1.8.1.8. Other soft tissue sarcomas of genitourinary tract

Hanley KZ, Birdsong GG, Mosunjac MB. Recent Developments in Surgical Pathology of the Uterine Corpus. Archives of pathology & laboratory medicine. 2017;141(4):528-41. Epub 2017/04/06. doi: https://doi.org/10.1007/s12098-017-2315-3 10.5858/arpa.2016-0284-SA. PubMed PMID: 28353387.

Yang W, Liu A, Wu J, Niu M. Prostatic stromal sarcoma: A case report and literature review. Medicine. 2018;97(18):e0495. Epub 2018/05/03. doi: https://doi.org/10.1097/md.0000000000010495. PubMed PMID: 29718840.

Wang P, Li Q, Zhang L, Ji H, Zhang CZ, Wang B. A myeloid sarcoma involving the small intestine, kidneys, mesentery, and mesenteric lymph nodes: A case report and literature review. Medicine. 2017;96(42):e7934. Epub 2017/10/20. doi: https://doi.org/10.1097/md.0000000000007934. PubMed PMID: 29049187; PubMed Central PMCID: PMCPmc5662353.

Shahin NA, Alqaisy A, Zheng W. Primary alveolar rhabdomyosarcoma of fallopian tube masquerading as a unilateral adnexal mass: A case report and literature review. Indian journal of pathology & microbiology. 2015;58(4):521-3. Epub 2015/11/10. doi: https://doi.org/10.4103/0377-4929.168884. PubMed PMID: 26549082.

Yoon JH, Ahn YH, Chun JI, Park HJ, Park BK. Acute Raoultella planticola cystitis in a child with rhabdomyosarcoma of the bladder neck. Pediatrics international : official journal of the Japan Pediatric Society. 2015;57(5):985-7. Epub 2015/10/29. doi: https://doi.org/10.1111/ped.12677. PubMed PMID: 26508180.

1.8.1.9. Soft tissue sarcoma of viscera

Blay JY, Brahmi M, Ray-Coquard I. European Journal of Cancer's Biennial report on soft tissue and visceral sarcomas or the rapid evolution of treatment concepts in sarcomas. European journal of cancer (Oxford, England : 1990). 2017;70:83-6. Epub 2016/11/28. doi: https://doi.org/10.1016/j.ejca.2016.07.028. PubMed PMID: 27889671.

Messiou C, Moskovic E, Vanel D, Morosi C, Benchimol R, Strauss D, et al. Primary retroperitoneal soft tissue sarcoma: Imaging appearances, pitfalls and diagnostic algorithm. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2017;43(7):1191-8. Epub 2017/01/07. doi: https://doi.org/10.1016/j.ejso.2016.10.032. PubMed PMID: 28057392.

Shang Leen SL, Fisher C, Thway K. Composite hemangioendothelioma: clinical and histologic features of an enigmatic entity. Advances in anatomic pathology. 2015;22(4):254-9. Epub 2015/06/08. doi: https://doi.org/10.1097/pap.0000000000000079. PubMed PMID: 26050262.

Englert D, Seal P, Parsons C, Arbour A, Roberts E, 3rd, Lopez FA. Clinical case of the month: a 22-year-old man with AIDS presenting with shortness of breath and an oral lesion. The Journal of the Louisiana State Medical Society : official organ of the Louisiana State Medical Society. 2014;166(5):224-30. Epub 2014/11/05. PubMed PMID: 25369228.

Gronchi A, Colombo C, Raut CP. Surgical management of localized soft tissue tumors. Cancer. 2014;120(17):2638-48. Epub 2014/04/23. doi: https://doi.org/10.1002/cncr.28715. PubMed PMID: 24752977.

1.8.1.10. Soft tissue sarcoma of paratestis

1.8.1.11. Soft tissue sarcoma of retroperitoneum and peritoneum

Almond LM, Gronchi A, Strauss D, Jafri M, Ford S, Desai A. Neoadjuvant and adjuvant strategies in retroperitoneal sarcoma. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2018;44(5):571-9. Epub 2018/02/24. doi: https://doi.org/10.1016/j.ejso.2018.02.001. PubMed PMID: 29472043.

Mandato VD, Torricelli F, Mastrofilippo V, Valli R, Aguzzoli L, La Sala GB. Primary extra-uterine and extra-ovarian mullerian adenosarcoma: case report and literature review. BMC cancer. 2018;18(1):134. Epub 2018/02/07. doi: https://doi.org/10.1186/s12885-018-4037-y. PubMed PMID: 29402239; PubMed Central PMCID: PMCPmc5800024.

Thway K, Jones RL, Noujaim J, Zaidi S, Miah AB, Fisher C. Dedifferentiated Liposarcoma: Updates on Morphology, Genetics, and Therapeutic Strategies. Advances in anatomic pathology. 2016;23(1):30-40. Epub 2015/12/10. doi: https://doi.org/10.1097/pap.0000000000000101. PubMed PMID: 26645460.

Schaefer IM, Fletcher CD. Diagnostically Challenging Spindle Cell Neoplasms of the Retroperitoneum. Surgical pathology clinics. 2015;8(3):353-74. Epub 2015/08/25. doi: https://doi.org/10.1016/j.path.2015.05.007. PubMed PMID: 26297061.

Vijay A, Ram L. Retroperitoneal liposarcoma: a comprehensive review. American journal of clinical oncology. 2015;38(2):213-9. Epub 2013/10/19. doi: https://doi.org/10.1097/COC.0b013e31829b5667. PubMed PMID: 24136142.

1.8.1.12. Soft tissue sarcoma of pelvis

Mullen JT, van Houdt W. Soft tissue tumors of the pelvis: Technical and histological considerations. Journal of surgical oncology. 2018;117(1):48-55. Epub 2017/12/22. doi: https://doi.org/10.1002/jso.24943. PubMed PMID: 29266252.

Parker WH. Indications for morcellation in gynecologic surgery. Current opinion in obstetrics & gynecology. 2018;30(1):75-80. Epub 2017/12/19. doi: https://doi.org/10.1097/gco.0000000000000427. PubMed PMID: 29251677.

Levy AD, Manning MA, Miettinen MM. Soft-Tissue Sarcomas of the Abdomen and Pelvis: Radiologic-Pathologic Features, Part 2-Uncommon Sarcomas. Radiographics : a review publication of the Radiological Society of North America, Inc. 2017;37(3):797-812. Epub 2017/05/17 doi: https://doi.org/10.1016/j.clon.2017.04.034 10.1148/rg.2017160201. PubMed PMID: 28493803.

He F, Zhang W, Shen Y, Yu P, Bao Q, Wen J, et al. Effects of resection margins on local recurrence of osteosarcoma in extremity and pelvis: Systematic review and meta-analysis. International journal of surgery (London, England). 2016;36(Pt A):283-92. Epub 2016/11/15. doi: https://doi.org/10.1016/j.ijsu.2016.11.016. PubMed PMID: 27840310.

Gaston CL, Sumathi VP, Grimer RJ. Is it ever safe to discharge a chondrosarcoma of pelvis? Report of a local recurrence after 10 years. Musculoskeletal surgery. 2014;98(3):241-6. Epub 2012/09/20. doi: https://doi.org/10.1007/s12306-012-0224-1. PubMed PMID: 22990984.

1.8.1.13. Soft tissue sarcoma of skin

Wei BR, Michael HT, Merlino G, Simpson RM, Martens MC, Seebode C, et al. Photocarcinogenesis and Skin Cancer Prevention Strategies: An Update. International journal of molecular sciences. 2018;38(2):1153-8. Epub 2018/02/02. doi: https://doi.org/10.3390/ijms19020394. PubMed PMID: 29374752; PubMed Central PMCID: PMCPmc5855616.

Bard RL. High-Frequency Ultrasound Examination in the Diagnosis of Skin Cancer. Dermatologic clinics. 2017;35(4):505-11. Epub 2017/09/10. doi: https://doi.org/10.1016/j.det.2017.06.011. PubMed PMID: 28886806.

Fort M, Guet S, Colson-Durand L, Auzolle C, Belkacemi Y. Role of radiation therapy in non-melanoma cancers, lymphomas and sarcomas of the skin: Systematic review and best practice in 2016. Critical reviews in oncology/hematology. 2016;99:200-13. Epub 2016/02/04. doi: https://doi.org/10.1016/j.critrevonc.2016.01.001. PubMed PMID: 26839172.

Gandhi SA, Kampp J. Skin Cancer Epidemiology, Detection, and Management. The Medical clinics of North America. 2015;99(6):1323-35. Epub 2015/10/18. doi: https://doi.org/10.1016/j.mcna.2015.06.002. PubMed PMID: 26476255.

Humphreys TR, Shah K, Wysong A, Lexa F, MacFarlane D. The role of imaging in the management of patients with nonmelanoma skin cancer: When is imaging necessary? Journal of the American Academy of Dermatology. 2017;76(4):591-607. Epub 2017/03/23. doi: https://doi.org/10.1016/j.jaad.2015.10.009. PubMed PMID: 28325389.

1.8.1.14. Soft tissue sarcoma of paraorbit

1.8.1.15. Soft tissue sarcoma of brain and other parts of nervous system

Kitamura Y, Sasaki H, Yoshida K. Genetic aberrations and molecular biology of skull base chordoma and chondrosarcoma. Brain tumor pathology. 2017;34(2):78-90. Epub 2017/04/30. doi: https://doi.org/10.1016/j.wneu.2017.04.100 10.1007/s10014-017-0283-y. PubMed PMID: 28432450.

Wimmer K, Rosenbaum T, Messiaen L. Connections between constitutional mismatch repair deficiency syndrome and neurofibromatosis type 1. Clinical genetics. 2017;91(4):507-19. Epub 2016/10/26. doi: https://doi.org/10.1111/cge.12904. PubMed PMID: 27779754.

Yamanaka R, Hayano A. Radiation-Induced Sarcomas of the Central Nervous System: A Systematic Review. World neurosurgery. 2017;98:818-28.e7. Epub 2016/12/14. doi: https://doi.org/10.1007/s00381-016-3318-5

Wirsching HG, Galanis E, Weller M. Glioblastoma. Handbook of clinical neurology. 2016;134:381-97. Epub 2016/03/08. doi: https://doi.org/10.1016/b978-0-12-802997-8.00023-2. PubMed PMID: 26948367.

Chen CJ, Williams EA, McAneney TE, Williams BJ, Mandell JW, Shaffrey ME. Histiocytic sarcoma of the cavernous sinus: case report and literature review. Brain tumor pathology. 2015;32(1):66-71. Epub 2014/05/09. doi: https://doi.org/10.1007/s10014-014-0191-3. PubMed PMID: 24807104.

1.8.1.16. Embryonal rhabdomyosarcoma of soft tissue

Peters SM, Kunkle T, Perrino MA, Philipone EM, Yoon AJ. Mandibular embryonal rhabdomyosarcoma with cartilaginous metaplasia: report of a case and review of literature. Oral surgery, oral medicine, oral pathology and oral radiology. 2017;124(6):e288-e93. Epub 2017/10/17. doi: https://doi.org/10.1016/j.oooo.2017.08.014. PubMed PMID: 29029988.

Panda SP, Chinnaswamy G, Vora T, Prasad M, Bansal D, Kapoor G, et al. Diagnosis and Management of Rhabdomyosarcoma in Children and Adolescents: ICMR Consensus Document. Indian journal of pediatrics. 2017;84(5):393-402. Epub 2017/04/06. doi: https://doi.org/10.1007/s12098-017-2315-3. PubMed PMID: 28378141.

van der Graaf WT, Orbach D, Judson IR, Ferrari A. Soft tissue sarcomas in adolescents and young adults: a comparison with their paediatric and adult counterparts. The Lancet Oncology. 2017;18(3):e166-e75. Epub 2017/03/09. doi: https://doi.org/10.1016/s1470-2045(17)30099-2. PubMed PMID: 28271871.

Cordoba Rovira SM, Inarejos Clemente EJ. Childhood rhabdomyosarcoma. Radiologia. 2016;58(6):481-90. Epub 2016/11/05. doi: https://doi.org/10.1016/j.rx.2016.09.003. PubMed PMID: 27810092.

Monti E, Fanzani A. Uncovering metabolism in rhabdomyosarcoma. Cell cycle (Georgetown, Tex). 2016;15(2):184-95. Epub 2015/07/26. doi: https://doi.org/10.1080/15384101.2015.1071746. PubMed PMID: 26209235; PubMed Central PMCID: PMCPmc4825834.

1.8.1.17. Alveolar rhabdomyosarcoma of soft tissue

Panda SP, Chinnaswamy G, Vora T, Prasad M, Bansal D, Kapoor G, et al. Diagnosis and Management of Rhabdomyosarcoma in Children and Adolescents: ICMR Consensus Document. Indian journal of

pediatrics. 2017;84(5):393-402. Epub 2017/04/06. doi: https://doi.org/10.1007/s12098-017-2315-3. PubMed PMID: 28378141.

van der Graaf WT, Orbach D, Judson IR, Ferrari A. Soft tissue sarcomas in adolescents and young adults: a comparison with their paediatric and adult counterparts. The Lancet Oncology. 2017;18(3):e166-e75. Epub 2017/03/09. doi: https://doi.org/10.1016/s1470-2045(17)30099-2. PubMed PMID: 28271871.

Liu H, Zhao W, Huang M, Zhou X, Gong Y, Lu Y. Alveolar rhabdomyosarcoma of nasopharynx and paranasal sinuses with metastasis to breast in a middle-aged woman: a case report and literature review. International journal of clinical and experimental pathology. 2015;8(11):15316-21. Epub 2016/01/30. PubMed PMID: 26823887; PubMed Central PMCID: PMCPmc4713673.

Picarsic J, Reyes-Mugica M. Phenotype and immunophenotype of the most common pediatric tumors. Applied immunohistochemistry & molecular morphology : AIMM. 2015;23(5):313-26. Epub 2014/11/13. doi: https://doi.org/10.1097/pai.0000000000000068. PubMed PMID: 2539035714.

Parham DM, Barr FG. Classification of rhabdomyosarcoma and its molecular basis. Advances in anatomic pathology. 2013;20(6):387-97. Epub 2013/10/12. doi: https://doi.org/10.1097/PAP.0b013e3182a92d0d. PubMed PMID: 24113309.

1.8.1.18. Ewin's sarcoma of soft tissue

Takami H, Kumar R, Brown DA, Krauss WE. Histologic Features and Prognosis of Spinal Intradural Extramedullary Ewing Sarcoma: Case Report, Literature Review, and Analysis of Prognosis. World neurosurgery. 2018;115:448-52.e2. Epub 2018/04/15. doi: https://doi.org/10.1016/j.wneu.2018.04.015. PubMed PMID: 29654955.

Theisen ER, Pishas KI, Saund RS, Lessnick SL. Therapeutic opportunities in Ewing sarcoma: EWS-FLI inhibition via LSD1 targeting. Oncotarget. 2016;7(14):17616-30. Epub 2016/02/06. doi: https://doi.org/10.18632/oncotarget.7124. PubMed PMID: 26848860; PubMed Central PMCID: PMCPmc4951237.

van Maldegem AM, Bovee JV, Peterse EF, Hogendoorn PC, Gelderblom H. Ewing sarcoma: The clinical relevance of the insulin-like growth factor 1 and the poly-ADP-ribose-polymerase pathway. European journal of cancer (Oxford, England : 1990). 2016;53:171-80. Epub 2016/01/15. doi: https://doi.org/10.1016/j.ejca.2015.09.009. PubMed PMID: 26765686.

Sand LG, Szuhai K, Hogendoorn PC. Sequencing Overview of Ewing Sarcoma: A Journey across Genomic, Epigenomic and Transcriptomic Landscapes. International journal of molecular sciences. 2015;16(7):16176-215. Epub 2015/07/21. doi: https://doi.org/10.3390/ijms160716176. PubMed PMID: 26193259; PubMed Central PMCID: PMCPmc4519945.

Todorova R. Ewing's sarcoma cancer stem cell targeted therapy. Current stem cell research & therapy. 2014;9(1):46-62. Epub 2013/12/04. PubMed PMID: 24294922.

1.8.2. Bone sarcoma

1.8.2.1. Osteogenic sarcoma

Zhang T, Zhang S, Yang F, Wang L, Zhu S, Qiu B, et al. Efficacy Comparison of Six Chemotherapeutic Combinations for Osteosarcoma and Ewing's Sarcoma Treatment: A Network Meta-Analysis. 2018;119(1):250-9. doi: https://doi.org/10.1002/jcb.25976. PubMed PMID: 28266080.

Brown HK, Tellez-Gabriel M, Heymann D. Cancer stem cells in osteosarcoma. Cancer letters. 2017;386:189-95. Epub 2016/11/30. doi: https://doi.org/10.1016/j.canlet.2016.11.019. PubMed PMID: 27894960.

Zreik RT, Meyer RG, Jenkins RB, Norambuena GA, Fritchie KJ. A Rare Pediatric Example of Subcutaneous Extraskeletal Osteosarcoma: A Case Report and Review of the Morphologic Differential Diagnosis. The

American Journal of dermatopathology. 2016;38(4):e44-8. Epub 2015/10/16. doi: https://doi.org/10.1097/dad.0000000000000458. PubMed PMID: 26460626.

Zhang Y, Ding C, Wang J, Sun G, Cao Y, Xu L, et al. Prognostic significance of CD44V6 expression in osteosarcoma: a meta-analysis. Journal of orthopaedic surgery and research. 2015;10:187. Epub 2015/12/25. doi: https://doi.org/10.1186/s13018-015-0328-z. PubMed PMID: 26697855; PubMed Central PMCID: PMCPmc4690422.

Botter SM, Neri D, Fuchs B. Recent advances in osteosarcoma. Current opinion in pharmacology. 2014;16:15-23. Epub 2014/03/19. doi: https://doi.org/10.1016/j.coph.2014.02.002. PubMed PMID: 24632219.

1.8.2.2. Chondrogenic sarcomas

Boehme KA, Schleicher SB, Traub F. Chondrosarcoma: A Rare Misfortune in Aging Human Cartilage? The Role of Stem and Progenitor Cells in Proliferation, Malignant Degeneration and Therapeutic Resistance. 2018;19(1). doi: https://doi.org/10.3390/ijms19010311. PubMed PMID: 29361725.

Rolauffs B, Tinoco G, Wilky BA, Paz-Mejia A, Rosenberg A, Trent JC. The biology and management of cartilaginous tumors: a role for targeting isocitrate dehydrogenase. International journal of molecular sciences. 2015:e648-55. Epub 2018/01/25 doi: https://doi.org/10.3390/ijms19010311 PubMed Central PMCID: PMCPmc5796255.

1.8.2.3. Notochordal sarcomas chordoma

Frankl J, Grotepas C, Stea B, Lemole GM, Chiu A, Khan R. Chordoma dedifferentiation after proton beam therapy: a case report and review of the literature. Journal of medical case reports. 2016;10(1):280. Epub 2016/10/13. doi: https://doi.org/10.1186/s13256-016-1076-3. PubMed PMID: 27729085; PubMed Central PMCID: PMCPmc5059891.

Kato S, Gasbarrini A, Ghermandi R, Gambarotti M, Bandiera S. Spinal chordomas dedifferentiated to osteosarcoma: a report of two cases and a literature review. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2016;25 Suppl 1:251-6. Epub 2016/04/08. doi: https://doi.org/10.1007/s00586-016-4557-6. PubMed PMID: 27052403.

1.8.2.4. Vascular sarcomas

Wang JG, Liu B, Gao H, Li YJ, Zhao P, Liu XP. Primary Cardiac Osteosarcoma. Heart, lung & circulation. 2016;25(7):698-704. Epub 2016/02/26. doi: https://doi.org/10.1016/j.hlc.2016.01.006. PubMed PMID: 26907617.

Wick MR. Contributions of Dr. Juan Rosai to the pathology of cutaneous vascular proliferations: A review of selected lesions. Seminars in diagnostic pathology. 2016;33(5):284-93. Epub 2016/06/20. doi: https://doi.org/10.1053/j.semdp.2016.05.010. PubMed PMID: 27318413.

Wong YP, Chia WK, Low SF, Mohamed-Haflah NH, Sharifah NA. Dendritic fibromyxolipoma: a variant of spindle cell lipoma with extensive myxoid change, with cytogenetic evidence. Pathology international. 2014;64(7):346-51. Epub 2014/07/23. doi: https://doi.org/10.1111/pin.12176. PubMed PMID: 25047505.

Hart JL, Edgar MA, Gardner JM. Vascular tumors of bone. Seminars in diagnostic pathology. 2014;31(1):30-8. Epub 2014/04/01. doi: https://doi.org/10.1053/j.semdp.2014.01.003. PubMed PMID: 24680180.

Antonescu C. Malignant vascular tumors—an update. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2014;27 Suppl 1:S30-8. Epub 2014/01/05. doi: https://doi.org/10.1038/modpathol.2013.176. PubMed PMID: 24384851.

1.8.2.5. Ewing's sarcoma

de Alava E. Ewing Sarcoma, an Update on Molecular Pathology with Therapeutic Implications. Surgical pathology clinics. 2017;10(3):575-85. Epub 2017/08/12. doi: https://doi.org/10.1016/j.path.2017.04.001. PubMed PMID: 28797503.

Bae SH, Hwang JH, Da Nam B, Kim HJ, Kim KU, Kim DW, et al. Multiple Ewing Sarcoma/Primitive Neuroectodermal Tumors in the Mediastinum: A Case Report and Literature Review. Medicine. 2016;95(7):e2725. Epub 2016/02/18. doi: https://doi.org/10.1097/md.0000000000002725. PubMed PMID: 26886614; PubMed Central PMCID: PMCPmc4998614.

Gaspar N, Hawkins DS, Dirksen U, Lewis IJ, Ferrari S, Le Deley MC, et al. Ewing Sarcoma: Current Management and Future Approaches Through Collaboration. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2015;33(27):3036-46. Epub 2015/08/26. doi: https://doi.org/10.1200/jco.2014.59.5256. PubMed PMID: 26304893.

Yoon JH, Kim H, Lee JW, Kang HJ, Park HJ, Park KD, et al. Ewing sarcoma/peripheral primitive neuroectodermal tumor in the adrenal gland of an adolescent: a case report and review of the literature. Journal of pediatric hematology/oncology. 2014;36(7):e456-9. Epub 2013/11/28. doi: https://doi.org/10.1097/mph.0000000000000058. PubMed PMID: 24276043.

Choi EY, Gardner JM, Lucas DR, McHugh JB, Patel RM. Ewing sarcoma. Seminars in diagnostic pathology. 2014;31(1):39-47. Epub 2014/04/01. doi: https://doi.org/10.1053/j.semdp.2014.01.002. PubMed PMID: 24680181.

1.8.2.6. Epithelial tumours adamantinoma

Wick MR. Primary lesions that may imitate metastatic tumors histologically: A selective review. Seminars in diagnostic pathology. 2018;35(2):123-42. Epub 2017/11/28. doi: https://doi.org/10.1053/j.semdp.2017.11.010. PubMed PMID: 29174934.

Lezcano C, Clarke MR, Zhang L, Antonescu CR, Seethala RR. Adamantinoma-like Ewing sarcoma mimicking basal cell adenocarcinoma of the parotid gland: a case report and review of the literature. Head and neck pathology. 2015;9(2):280-5. Epub 2014/08/02. doi: https://doi.org/10.1007/s12105-014-0558-0. PubMed PMID: 25081914; PubMed Central PMCID: PMCPmc4424212.

1.8.2.7. Other high grade sarcomas (fibrosarcoma malignant fibrous histiocytoma)

Green B, Godden D, Brennan PA. Malignant cutaneous adnexal tumours of the head and neck: an update on management. The British journal of oral & maxillofacial surgery. 2015;53(6):485-90. Epub 2015/04/26. doi: https://doi.org/10.1016/j.bjoms.2015.03.005. PubMed PMID: 25911053.

Hourani R, Taslakian B, Shabb NS, Nassar L, Hourani MH, Moukarbel R, et al. Fibroblastic and myofibroblastic tumors of the head and neck: comprehensive imaging-based review with pathologic correlation. European journal of radiology. 2015;84(2):250-60. Epub 2014/12/04. doi: https://doi.org/10.1016/j.ejrad.2014.10.017. PubMed PMID: 25467227.

Qu N, Yao W, Cui X, Zhang H. Malignant transformation in monostotic fibrous dysplasia: clinical features, imaging features, outcomes in 10 patients, and review. Medicine. 2015;94(3):e369. Epub 2015/01/27. doi: https://doi.org/10.1097/md.0000000000000369. PubMed PMID: 25621678; PubMed Central PMCID: PMCPmc4602648.

Samaratunga H, Delahunt B. Mesenchymal tumors of adult kidney. Seminars in diagnostic pathology. 2015;32(2):160-71. Epub 2015/03/17. doi: https://doi.org/10.1053/j.semdp.2015.02.007. PubMed PMID: 25773128.

Surov A, Gottschling S, Wienke A, Meyer HJ, Spielmann RP, Dralle H. Primary Thyroid Sarcoma: A Systematic Review. Anticancer research. 2015;35(10):5185-91. Epub 2015/09/27. PubMed PMID: 26408676.

1.8.3. Gastrointestinal stromal sarcoma

Wozniak A, Gebreyohannes YK, Debiec-Rychter M, Schoffski P. New targets and therapies for gastrointestinal stromal tumors. Expert review of anticancer therapy. 2017;17(12):1117-29. Epub 2017/11/08. doi: https://doi.org/10.1080/14737140.2017.1400386. PubMed PMID: 29110548.

Watson GA, Kelly D, Melland-Smith M, Gleeson J, McEntee G, Kelly CM, et al. Get the GIST? An overview of gastrointestinal stromal tumours. Irish journal of medical science. 2016;185(2):319-26. Epub 2016/02/03. doi: https://doi.org/10.1007/s11845-016-1410-1. PubMed PMID: 26833487.

Bhatt NR, Collins D, Crotty P, Ridgway PF. Prognosis and management of adult wild type gastrointestinal stromal tumours (GISTs): A pooled analysis and review of literature. Surgical oncology. 2016;25(3):152-7. Epub 2016/08/28. doi: https://doi.org/10.1016/j.suronc.2016.05.003. PubMed PMID: 27566016.

Akcakaya P, Lui WO. MicroRNAs and Gastrointestinal Stromal Tumor. Advances in experimental medicine and biology. 2015;889:51-70. Epub 2015/12/15. doi: https://doi.org/10.1007/978-3-319-23730-5_4. PubMed PMID: 26658996.

Yamamoto H, Oda Y. Gastrointestinal stromal tumor: recent advances in pathology and genetics. Pathology international. 2015;65(1):9-18. Epub 2014/11/22. doi: https://doi.org/10.1111/pin.12230. PubMed PMID: 25414046.

1.9. Digestive rare cancers

1.9.1. Epithelial tumours of oesophagus

Zhang W, Wang DH. Origins of Metaplasia in Barrett's Esophagus: Is this an Esophageal Stem or Progenitor Cell Disease? Digestive diseases and sciences. 2018;63(8):2005-12. Epub 2018/04/21. doi: https://doi.org/10.1007/s10620-018-5069-5. PubMed PMID: 29675663.

Montagnani F, Fornaro L, Frumento P, Vivaldi C, Falcone A, Fioretto L. Multimodality treatment of locally advanced squamous cell carcinoma of the oesophagus: A comprehensive review and network meta-analysis. Critical reviews in oncology/hematology. 2017;114:24-32. Epub 2017/05/10. doi: https://doi.org/10.1016/j.critrevonc.2017.03.024. PubMed PMID: 28477744.

Xu B, Zhou X, Li X, Liu C, Yang C. Diabetes mellitus carries a risk of esophageal cancer: A meta-analysis. Medicine. 2017;96(35):e7944. Epub 2017/09/01. doi: https://doi.org/10.1097/md.0000000000007944. PubMed PMID: 28858123; PubMed Central PMCID: PMCPmc5585517.

Yazbeck R, Jaenisch SE, Watson DI. From blood to breath: New horizons for esophageal cancer biomarkers. World journal of gastroenterology. 2016;22(46):10077-83. Epub 2016/12/29. doi: https://doi.org/10.3748/wjg.v22.i46.10077. PubMed PMID: 28028355; PubMed Central PMCID: PMCPmc5155166.

Hayakawa Y, Sethi N, Sepulveda AR, Bass AJ, Wang TC. Oesophageal adenocarcinoma and gastric cancer: should we mind the gap? Nature reviews Cancer. 2016;16(5):305-18. Epub 2016/04/27. doi: https://doi.org/10.1038/nrc.2016.24. PubMed PMID: 27112208.

1.9.1.1. Squamous cell carcinoma with variants of oesophagus

1.9.1.2. Adenocarcinoma with variants of oesophagus

1.9.1.3. Salivary gland type tumours of oesophagus

1.9.1.4. Undifferentiated carcinoma of oesophagus

1.9.2. Rare epithelial tumours of stomach

Ye W, Tang Y, Yao C, Shi J, Xu Y, Jiang J. Advanced gastrointestinal carcinoma with massive ascites and hydrothorax during pregnancy: A case report and review of the literature. Medicine. 2017;96(51):e9354. Epub 2018/02/03. doi: https://doi.org/10.1097/md.0000000000009354. PubMed PMID: 29390520; PubMed Central PMCID: PMCPmc5758222.

Yoshizawa J, Ishizone S, Ikeyama M, Nakayama J. Gastric hepatoid adenocarcinoma resulting in a spontaneous gastric perforation: a case report and review of the literature. BMC cancer. 2017;17(1):368. Epub 2017/05/27. doi: https://doi.org/10.1186/s12885-017-3357-7. PubMed PMID: 28545511; PubMed Central PMCID: PMCPmc5445331.

Yamashita K, Hosoda K, Ema A, Watanabe M. Lymph node ratio as a novel and simple prognostic factor in advanced gastric cancer. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2016;42(9):1253-60. Epub 2016/03/28. doi: https://doi.org/10.1016/j.ejso.2016.03.001. PubMed PMID: 27017273.

Yang LH, Wang JO, Ma S, Zhu Z, Sun JX, Ding SL, et al. Synchronous of gastric adenocarcinoma and schwannoma: report of a case and review of literatures. International journal of clinical and experimental pathology. 2015;8(1):1041-5. Epub 2015/03/11. PubMed PMID: 25755816; PubMed Central PMCID: PMCPmc4348807.

Zeng YJ, Zhang CD, Dai DQ. Impact of lymph node micrometastasis on gastric carcinoma prognosis: a meta-analysis. World journal of gastroenterology. 2015;21(5):1628-35. Epub 2015/02/11. doi: https://doi.org/10.3748/wjg.v21.i5.1628. PubMed PMID: 25663783; PubMed Central PMCID: PMCPmc4316106.

1.9.2.1. Squamous cell carcinoma with variants of stomach

1.9.2.2. Salivary gland-type tumours of stomach

1.9.2.3. Undifferentiated carcinoma of stomach

1.9.3. Epithelial tumours of small intestine

Zhao Y, Yang X, Ye Y. Adenocarcinoma located at a Meckel's Diverticulum: A case report and literature review. Journal of cancer research and therapeutics. 2017;13(5):878-81. Epub 2017/12/15. doi: https://doi.org/10.4103/jcrt.JCRT_124_17. PubMed PMID: 29237920.

Suh CH, Tirumani SH, Shinagare AB, Kim KW, Rosenthal MH, Ramaiya NH, et al. Diagnosis and management of duodenal adenocarcinomas: a comprehensive review for the radiologist. Abdominal imaging. 2015;40(5):1110-20. Epub 2014/11/28. doi: https://doi.org/10.1007/s00261-014-0309-4. PubMed PMID: 25427987.

Tesfay M, Xianzhong DD, Poddar N. Unusual case of primary adenocarcinoma of the small bowel and lung occurring in a patient: a case report and review of literature. Journal of gastrointestinal cancer. 2015;46(1):80-4. Epub 2014/12/30. doi: https://doi.org/10.1007/s12029-014-9677-9. PubMed PMID: 25544364.

Van Weyenberg SJ, Mulder CJ, Van Waesberghe JH. Small bowel imaging in celiac disease. Digestive diseases (Basel, Switzerland). 2015;33(2):252-9. Epub 2015/05/01. doi: https://doi.org/10.1159/000369516. PubMed PMID: 25925931.

Zaaimi Y, Aparicio T, Laurent-Puig P, Taieb J, Zaanan A. Advanced small bowel adenocarcinoma: Molecular characteristics and therapeutic perspectives. Clinics and research in hepatology and gastroenterology. 2016;40(2):154-60. Epub 2015/11/09. doi: https://doi.org/10.1016/j.clinre.2015.09.008. PubMed PMID: 26547136.

1.9.3.1. Adenocarcinoma with variants of small intestine

1.9.3.2. Squamous cell carcinoma with variants of small intestine

1.9.4. Rare epithelial tumours of colon

Shaib WL, Assi R, Shamseddine A, Alese OB, Staley C, 3rd, Memis B, et al. Appendiceal Mucinous Neoplasms: Diagnosis and Management. The oncologist. 2017;22(9):1107-16. Epub 2017/07/01. doi:

https://doi.org/10.1634/theoncologist.2017-0081. PubMed PMID: 28663356; PubMed Central PMCID: PMCPmc5599200.

Yu X, Wang Z, Zhang Z, Liu Y, Huang J. Postoperation of cervical cancer with intestine metastasis: a case report and literature review. World journal of surgical oncology. 2016;14(1):2. Epub 2016/01/08. doi: https://doi.org/10.1186/s12957-015-0759-3. PubMed PMID: 26739660; PubMed Central PMCID: PMCPmc4704422.

Vandevelde A, Gera P. Carcinoid tumours of the appendix in children having appendicectomies at Princess Margaret Hospital since 1995. Journal of pediatric surgery. 2015;50(9):1595-9. Epub 2015/08/12. doi: https://doi.org/10.1016/j.jpedsurg.2015.06.002. PubMed PMID: 26259557

Legitimo A, Consolini R, Failli A, Orsini G, Spisni R. Dendritic cell defects in the colorectal cancer. Human vaccines & immunotherapeutics. 2014;10(11):3224-35. Epub 2014/12/09. doi: https://doi.org/10.4161/hv.29857. PubMed PMID: 25483675; PubMed Central PMCID: PMCPmc4514061.

Xu F, Feng GS, Wang ZJ, Zhang KN. Synchronous double cancers of colonic large cell neuroendocrine carcinoma and gastric squamous-cell carcinoma: a case report and review of literature. International journal of clinical and experimental pathology. 2014;7(8):5177-80. Epub 2014/09/10. PubMed PMID: 25197393; PubMed Central PMCID: PMCPmc4152083.

1.9.4.1. Squamous cell carcinoma with variants of colon

1.9.4.2. Fibromixoma and low grade mucinous adenocarcinoma of the appendix

1.9.5. Rare epithelial tumours of rectum

Yu X, Wang Z, Zhang Z, Liu Y, Huang J. Postoperation of cervical cancer with intestine metastasis: a case report and literature review. World journal of surgical oncology. 2016;14(1):2. Epub 2016/01/08. doi: https://doi.org/10.1186/s12957-015-0759-3. PubMed PMID: 26739660; PubMed Central PMCID: PMCPmc4704422.3.

Garcia NA, Hernando Cubero J, Alonso Orduna V, Torrecilla Idoipe N, Calvo Escribano C, Fernandez Atuan R. Adenosquamous Cell Carcinoma of the Rectum in a Girl: First Case Reported and Review of the Literature. Journal of pediatric hematology/oncology. 2015;37(6):e364-7. Epub 2015/07/17. doi: https://doi.org/10.1097/mph.0000000000000361. PubMed PMID: 26181422.

Matalon SA, Mamon HJ, Fuchs CS, Doyle LA, Tirumani SH, Ramaiya NH, et al. Anorectal Cancer: Critical Anatomic and Staging Distinctions That Affect Use of Radiation Therapy. Radiographics : a review publication of the Radiological Society of North America, Inc. 2015;35(7):2090-107. Epub 2015/11/13. doi: https://doi.org/10.1148/rg.2015150037. PubMed PMID: 26562239; PubMed Central PMCID: PMCPmc4664281.

Errasti Alustiza J, Espin Basany E, Reina Duarte A. Rare tumors of the rectum. Narrative review. Cirugia espanola. 2014;92(9):579-88. Epub 2014/03/19. doi: https://doi.org/10.1016/j.ciresp.2013.06.019. PubMed PMID: 24629769.

Vinciguerra GL, Mercantini P, La Torre M, Pilozzi E, Ziparo V, Vecchione A. Transitional cell carcinoma of the retrorectal space arisen in tailgut cyst: a case report and review of the literature. International journal of surgical pathology. 2014;22(3):280-5. Epub 2013/07/03. doi: https://doi.org/10.1177/1066896913491324. PubMed PMID: 23816825.

1.9.5.1. Squamous cell carcinoma with variants of rectum

1.9.6. Epithelial tumours of anal canal

1.9.6.1. Squamous cell carcinoma with variants of anal canal

Martin D, Balermpas P, Winkelmann R, Rodel F, Rodel C, Fokas E. Anal squamous cell carcinoma - State of the art management and future perspectives. Cancer Treat Rev. 2018;65:11-21. doi: https://doi.org/10.1016/j.ctrv.2018.02.001. PubMed PMID: 29494827.

Kim SS, Kim GE, Ko AH. A Patient with HIV-Associated Metastatic Anal Squamous Cell Carcinoma Receiving Multimodality Therapy with Curative Intent: Case Report and Review of the Literature. J Gastrointest Cancer. 2017;48(1):94-9. doi: https://doi.org/10.1007/s12029-016-9814-8. PubMed PMID: 26961789.

Masab M, Saif MW. Anal Squamous Cell Carcinoma in a Patient with Myasthenia Gravis: Is Immunosuppression the Main Underlying Etiology? Cureus. 2017;9(11):e1845. doi: https://doi.org/10.7759/cureus.1845. PubMed PMID: 29348988; PubMed Central PMCID: PMCPMC5768322.

Osborne MC, Maykel J, Johnson EK, Steele SR. Anal squamous cell carcinoma: an evolution in disease and management. World J Gastroenterol. 2014;20(36):13052-9. doi: https://doi.org/10.3748/wjg.v20.i36.13052. PubMed PMID: 25278699; PubMed Central PMCID: PMCPMC4177484.

Tong WW, Hillman RJ, Kelleher AD, Grulich AE, Carr A. Anal intraepithelial neoplasia and squamous cell carcinoma in HIV-infected adults. HIV Med. 2014;15(2):65-76. doi: https://doi.org/10.1111/hiv.12080. PubMed PMID: 24007498.

1.9.6.2. Adenocarcinoma with variants of anal canal

Kulkarni MP, Momin YA, Pandav AB, Sulhyan KR. Adenocarcinoma of the anal canal: A report of two cases with review of literature. Indian J Pathol Microbiol. 2016;59(3):404-6. doi: https://doi.org/10.4103/0377-4929.188139. PubMed PMID: 27510691.

Tan JK, Teo NZ, Ong CJ, Yusof SB, Wijaya R. A Minimally Invasive Surgical Approach to Synchronous Anal and Colon Adenocarcinoma: Review of Existing Literature. Int J Colorectal Dis. 2016;31(8):1543-5. doi: https://doi.org/10.1007/s00384-016-2572-z. PubMed PMID: 27021612.

1.9.6.3. Paget's disease of anal canal

1.9.7. Rare epithelial tumours of pancras

1.9.7.1. Squamous cell carcinoma with variants of pancreas

Marcus R, Maitra A, Roszik J. Recent advances in genomic profiling of adenosquamous carcinoma of the pancreas. J Pathol. 2017;243(3):271-2. doi: https://doi.org/10.1002/path.4959. PubMed PMID: 28816351.

Ntanasis-Stathopoulos I, Tsilimigras DI, Georgiadou D, Kanavidis P, Riccioni O, Salla C, et al. Squamous cell carcinoma of the pancreas: A systematic review and pooled survival analysis. Eur J Cancer. 2017;79:193-204. doi: https://doi.org/10.1016/j.ejca.2017.04.006. PubMed PMID: 28511147.

Ben Kridis W, Khanfir A, Toumi N, Ben Amar M, Boudawara T, Frikha M. Primary squamous cell carcinoma of the pancreas: a report of two cases and review of the literature. Intern Med. 2015;54(11):1357-9. doi: https://doi.org/10.2169/internalmedicine.54.4091. PubMed PMID: 26027986.

Mehta M, Sinha J, Ogawa M, Ganguly A, Xiang D, Poddar N. Unusual Case of Squamous Cell Carcinoma of Pancreas with Review of Literature. J Gastrointest Cancer. 2015;46(4):426-9. doi: https://doi.org/10.1007/s12029-015-9712-5. PubMed PMID: 25894633.

Thomas D, Shah N, Shaaban H, Maroules M. An interesting clinical entity of squamous cell cancer of the pancreas with liver and bone metastases: a case report and review of the literature. J Gastrointest Cancer. 2014;45 Suppl 1:88-90. doi: https://doi.org/10.1007/s12029-013-9560-0. PubMed PMID: 24242860.

1.9.7.2. Acinar cell carcinoma of pancreas

Al-Hader A, Al-Rohil RN, Han H, Von Hoff D. Pancreatic acinar cell carcinoma: A review on molecular profiling of patient tumors. World J Gastroenterol. 2017;23(45):7945-51. doi: https://doi.org/10.3748/wjg.v23.i45.7945. PubMed PMID: 29259370; PubMed Central PMCID: PMCPMC5725289.

Luo Y, Hu G, Ma Y, Guo N, Li F. Acinar cell carcinoma of the pancreas presenting as diffuse pancreatic enlargement: Two case reports and literature review. Medicine (Baltimore). 2017;96(38):e7904. doi: https://doi.org/10.1097/MD.0000000000007904. PubMed PMID: 28930825; PubMed Central PMCID: PMCPMC5617692.

Glazer ES, Neill KG, Frakes JM, Coppola D, Hodul PJ, Hoffe SE, et al. Systematic Review and Case Series Report of Acinar Cell Carcinoma of the Pancreas. Cancer Control. 2016;23(4):446-54. doi: https://doi.org/10.1177/107327481602300417. PubMed PMID: 27842335.

Klimstra DS, Adsay V. Acinar neoplasms of the pancreas-A summary of 25 years of research. Semin Diagn Pathol. 2016;33(5):307-18. doi: https://doi.org/10.1053/j.semdp.2016.05.009. PubMed PMID: 27320062.

Wang Y, Wang S, Zhou X, Zhou H, Cui Y, Li Q, et al. Acinar cell carcinoma: a report of 19 cases with a brief review of the literature. World J Surg Oncol. 2016;14(1):172. doi: https://doi.org/10.1186/s12957-016-0919-0. PubMed PMID: 27352960; PubMed Central PMCID: PMCPMC4924290.

1.9.7.3. Mucinous cystadenocarcinoma of pancreas

Al Efishat M, Allen PJ. Therapeutic Approach to Cystic Neoplasms of the Pancreas. Surg Oncol Clin N Am. 2016;25(2):351-61. doi: https://doi.org/10.1016/j.soc.2015.11.006. PubMed PMID: 27013369; PubMed Central PMCID: PMCPMC4991876.

Cahalane AM, Purcell YM, Lavelle LP, McEvoy SH, Ryan ER, O'Toole E, et al. Which is the best current guideline for the diagnosis and management of cystic pancreatic neoplasms? An appraisal using evidence-based practice methods. Eur Radiol. 2016;26(9):3121-8. doi: https://doi.org/10.1007/s00330-015-4160-y. PubMed PMID: 26762943.

Ketwaroo GA, Mortele KJ, Sawhney MS. Pancreatic Cystic Neoplasms: An Update. Gastroenterol Clin North Am. 2016;45(1):67-81. doi: https://doi.org/10.1016/j.gtc.2015.10.006. PubMed PMID: 26895681.

Nilsson LN, Keane MG, Shamali A, Millastre Bocos J, Marijinissen van Zanten M, Antila A, et al. Nature and management of pancreatic mucinous cystic neoplasm (MCN): A systematic review of the literature. Pancreatology. 2016;16(6):1028-36. doi: https://doi.org/10.1016/j.pan.2016.09.011. PubMed PMID: 27681503.

1.9.7.4. Intraductal papillary mucinous carcinoma invasive of pancreas

Pagliari D, Saviano A, Serricchio ML, Dal Lago AA, Brizi MG, Lanza F, et al. Uptodate in the assessment and management of intraductal papillary mucinous neoplasms of the pancreas. Eur Rev Med Pharmacol Sci. 2017;21(12):2858-74. PubMed PMID: 28682431.

Chelliah A, Kalimuthu S, Chetty R. Intraductal tubular neoplasms of the pancreas: an overview. Ann Diagn Pathol. 2016;24:68-72. doi: https://doi.org/10.1016/j.anndiagpath.2016.04.009. PubMed PMID: 27185640.

Nishi T, Kawabata Y, Ishikawa N, Araki A, Yano S, Maruyama R, et al. Intraductal papillary mucinous carcinoma of the pancreas associated with pancreas divisum: a case report and review of the literature. BMC Gastroenterol. 2015;15:78. doi: https://doi.org/10.1186/s12876-015-0313-3. PubMed PMID: 26152300; PubMed Central PMCID: PMCPMC4495851.

Sahora K, Fernandez-del Castillo C. Intraductal papillary mucinous neoplasms. Curr Opin Gastroenterol. 2015;31(5):424-9. doi: https://doi.org/10.1097/MOG.0000000000000198. PubMed PMID: 26125316.

Kloppel G, Basturk O, Schlitter AM, Konukiewitz B, Esposito I. Intraductal neoplasms of the pancreas. Semin Diagn Pathol. 2014;31(6):452-66. doi: https://doi.org/10.1053/j.semdp.2014.08.005. PubMed PMID: 25282472.

1.9.7.5. Solid pseudopapillary carcinoma of pancreas

Antoniou EA, Damaskos C, Garmpis N, Salakos C, Margonis GA, Kontzoglou K, et al. Solid Pseudopapillary Tumor of the Pancreas: A Single-center Experience and Review of the Literature. In Vivo. 2017;31(4):501-10. doi: https://doi.org/10.21873/invivo.11089. PubMed PMID: 28652415; PubMed Central PMCID: PMCPMC5566898.

Naar L, Spanomichou DA, Mastoraki A, Smyrniotis V, Arkadopoulos N. Solid Pseudopapillary Neoplasms of the Pancreas: A Surgical and Genetic Enigma. World J Surg. 2017;41(7):1871-81. doi: https://doi.org/10.1007/s00268-017-3921-y. PubMed PMID: 28251269.

Jakhlal N, Njoumi N, Hachi H, Bougtab A. [Solid pseudopapillary tumour of the pancreas: about a case and review of the literature]. Pan Afr Med J. 2016;24:104. doi: https://doi.org/10.11604/pamj.2016.24.104.8301. PubMed PMID: 27642443; PubMed Central PMCID: PMCPMC5012806.

Law JK, Ahmed A, Singh VK, Akshintala VS, Olson MT, Raman SP, et al. A systematic review of solid-pseudopapillary neoplasms: are these rare lesions? Pancreas. 2014;43(3):331-7. doi: https://doi.org/10.1097/MPA.0000000000000061. PubMed PMID: 24622060; PubMed Central PMCID: PMCPMC4888067.

Yener AN, Manukyan M, Midi A, Cubuk R. Solid pseudopapillary neoplasm of the pancreas: report of a rare case and review of the literature. Turk Patoloji Derg. 2014;30(3):228-32. doi: https://doi.org/10.5146/tjpath.2013.01192. PubMed PMID: 24101358.

1.9.7.6. Serous cystadenocarcinoma of pancreas

Van Dyke TJ, Johlin FC, Bellizzi AM, Howe JR. Serous Cystadenocarcinoma of the Pancreas: Clinical Features and Management of a Rare Tumor. Dig Surg. 2016;33(3):240-8. doi: https://doi.org/10.1159/000444721. PubMed PMID: 26998825.

Antonini F, Fuccio L, Fabbri C, Macarri G, Palazzo L. Management of serous cystic neoplasms of the pancreas. Expert Rev Gastroenterol Hepatol. 2015;9(1):115-25. doi: https://doi.org/10.1586/17474124.2014.934675. PubMed PMID: 24981593.

Reid MD, Choi HJ, Memis B, Krasinskas AM, Jang KT, Akkas G, et al. Serous Neoplasms of the Pancreas: A Clinicopathologic Analysis of 193 Cases and Literature Review With New Insights on Macrocystic and Solid Variants and Critical Reappraisal of So-called „Serous Cystadenocarcinoma". Am J Surg Pathol. 2015;39(12):1597-610. doi: https://doi.org/10.1097/PAS.0000000000000559. PubMed PMID: 26559376.

Al-Jiffry BO, Rayzah F, Khayat SH. A disseminated variant of pancreatic serous cystadenoma causing obstructive jaundice, a very rare entity: a case report and review of the literature. BMC Res Notes. 2014;7:749. doi: https://doi.org/10.1186/1756-0500-7-749. PubMed PMID: 25338636; PubMed Central PMCID: PMCPMC4213478.

Reid MD, Choi H, Balci S, Akkas G, Adsay V. Serous cystic neoplasms of the pancreas: clinicopathologic and molecular characteristics. Semin Diagn Pathol. 2014;31(6):475-83. doi: https://doi.org/10.1053/j.semdp.2014.08.009. PubMed PMID: 25441309.

1.9.7.7. Carcinoma with osteoclast-like giant cells of pancreas

Gao HQ, Yang YM, Zhuang Y, Liu P. Locally advanced undifferentiated carcinoma with osteoclast-like giant cells of the pancreas. World J Gastroenterol. 2015;21(2):694-8. doi: https://doi.org/10.3748/wjg.v21.i2.694. PubMed PMID: 25593500; PubMed Central PMCID: PMCPMC4292306.

Sah SK, Li Y, Li Y. Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells: a rare case report and review of the literature. Int J Clin Exp Pathol. 2015;8(9):11785-91. PubMed PMID: 26617927; PubMed Central PMCID: PMCPMC4637743.

Jo S. Huge undifferentiated carcinoma of the pancreas with osteoclast-like giant cells. World J Gastroenterol. 2014;20(10):2725-30. doi: https://doi.org/10.3748/wjg.v20.i10.2725. PubMed PMID: 24627610; PubMed Central PMCID: PMCPMC3949283.

1.9.8. Epithelial tumours of liver and intrahepatic bile tract (IBT)

1.9.8.1. Hepatocellular carcinoma of liver and IBT

Kulik L, Heimbach JK, Zaiem F, Almasri J, Prokop LJ, Wang Z, et al. Therapies for patients with hepatocellular carcinoma awaiting liver transplantation: A systematic review and meta-analysis. Hepatology. 2018;67(1):381-400. doi: https://doi.org/10.1002/hep.29485. PubMed PMID: 28859222.

Ma C, Zhang Q, Greten TF. Nonalcoholic fatty liver disease promotes hepatocellular carcinoma through direct and indirect effects on hepatocytes. FEBS J. 2018;285(4):752-62. doi: https://doi.org/10.1111/febs.14209. PubMed PMID: 28857485.

Rudnick SR, Russo MW. Liver transplantation beyond or downstaging within the Milan criteria for hepatocellular carcinoma. Expert Rev Gastroenterol Hepatol. 2018;12(3):265-75. doi: https://doi.org/10.1080/17474124.2018.1417035. PubMed PMID: 29231769.

Sparchez Z, Mocan T. Contemporary role of liver biopsy in hepatocellular carcinoma. World J Hepatol. 2018;10(7):452-61. doi: https://doi.org/10.4254/wjh.v10.i7.452. PubMed PMID: 30079131; PubMed Central PMCID: PMCPMC6068845.

Stine JG, Wentworth BJ, Zimmet A, Rinella ME, Loomba R, Caldwell SH, et al. Systematic review with meta-analysis: risk of hepatocellular carcinoma in non-alcoholic steatohepatitis without cirrhosis compared to other liver diseases. Aliment Pharmacol Ther. 2018. doi: https://doi.org/10.1111/apt.14937. PubMed PMID: 30136293.

1.9.8.2. Hepatocellular carcinoma fibrolamellar of liver and IBT

Kassahun WT. Contemporary management of fibrolamellar hepatocellular carcinoma: diagnosis, treatment, outcome, prognostic factors, and recent developments. World J Surg Oncol. 2016;14(1):151. doi: https://doi.org/10.1186/s12957-016-0903-8. PubMed PMID: 27215576; PubMed Central PMCID: PMCPMC4877801.

Riggle KM, Turnham R, Scott JD, Yeung RS, Riehle KJ. Fibrolamellar Hepatocellular Carcinoma: Mechanistic Distinction From Adult Hepatocellular Carcinoma. Pediatr Blood Cancer. 2016;63(7):1163-7. doi: https://doi.org/10.1002/pbc.25970. PubMed PMID: 26990031; PubMed Central PMCID: PMCPMC4877189.

Ganeshan D, Szklaruk J, Kundra V, Kaseb A, Rashid A, Elsayes KM. Imaging features of fibrolamellar hepatocellular carcinoma. AJR Am J Roentgenol. 2014;202(3):544-52. doi: https://doi.org/10.2214/AJR.13.11117. PubMed PMID: 24555590.

Lim, II, Farber BA, LaQuaglia MP. Advances in fibrolamellar hepatocellular carcinoma: a review. Eur J Pediatr Surg. 2014;24(6):461-6. doi: https://doi.org/10.1055/s-0034-1396420. PubMed PMID: 25486412.

Matsuda M, Amemiya H, Kawaida H, Okamoto H, Hosomura N, Asakawa M, et al. Typical fibrolamellar hepatocellular carcinoma in a Japanese boy: report of a case. Surg Today. 2014;44(7):1359-66. doi: https://doi.org/10.1007/s00595-013-0653-y. PubMed PMID: 23828653.

1.9.8.3. Cholangiocarcinoma of IBT

Gibiino G, Fabbri C, Fagiuoli S, Ianiro G, Fornelli A, Cennamo V. Defining the biology of intrahepatic cholangiocarcinoma: molecular pathways and early detection of precursor lesions. Eur Rev Med Pharmacol Sci. 2017;21(4):730-41. PubMed PMID: 28272710.

Massarweh NN, El-Serag HB. Epidemiology of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. Cancer Control. 2017;24(3):1073274817729245. doi: https://doi.org/10.1177/1073274817729245. PubMed PMID: 28975830; PubMed Central PMCID: PMCPMC5937247.

Oliveira IS, Kilcoyne A, Everett JM, Mino-Kenudson M, Harisinghani MG, Ganesan K. Cholangiocarcinoma: classification, diagnosis, staging, imaging features, and management. Abdom Radiol (NY). 2017;42(6):1637-49. doi: https://doi.org/10.1007/s00261-017-1094-7. PubMed PMID: 28271275.

Rahnemai-Azar AA, Weisbrod A, Dillhoff M, Schmidt C, Pawlik TM. Intrahepatic cholangiocarcinoma: Molecular markers for diagnosis and prognosis. Surg Oncol. 2017;26(2):125-37. doi: https://doi.org/10.1016/j.suronc.2016.12.009. PubMed PMID: 28577718.

Rahnemai-Azar AA, Weisbrod AB, Dillhoff M, Schmidt C, Pawlik TM. Intrahepatic cholangiocarcinoma: current management and emerging therapies. Expert Rev Gastroenterol Hepatol. 2017;11(5):439-49. doi: https://doi.org/10.1080/17474124.2017.1309290. PubMed PMID: 28317403.

1.9.8.4. Adenocarcinoma with variants of liver and IBT

1.9.8.5. Undifferentiated carcinoma of liver and IBT

1.9.8.6. Squamous cell carcinoma with variants of liver and IBT

Montagnana M, Danese E, Lippi G. Squamous cell carcinoma antigen in hepatocellular carcinoma: Ready for the prime time? Clin Chim Acta. 2015;445:161-6. doi: https://doi.org/10.1016/j.cca.2015.03.031. PubMed PMID: 25840050.

Toe BP, Ramli N, Lam SY, Wong KT, Prepageran N. Basaloid squamous cell carcinoma of the sinonasal tract with metastasis to the liver: a case report and literature review. Ear Nose Throat J. 2015;94(2):E27-32. PubMed PMID: 25651356.

Zhang XF, Du ZQ, Liu XM, Lv Y. Primary Squamous Cell Carcinoma of Liver: Case Series and Review of Literatures. Medicine (Baltimore). 2015;94(28):e868. doi: https://doi.org/10.1097/MD.0000000000000868. PubMed PMID: 26181570; PubMed Central PMCID: PMCPMC4617094.

1.9.8.7. Bile duct cystadenocarcinoma of IBT

Soares KC, Arnaoutakis DJ, Kamel I, Anders R, Adams RB, Bauer TW, et al. Cystic neoplasms of the liver: biliary cystadenoma and cystadenocarcinoma. J Am Coll Surg. 2014;218(1):119-28. doi: https://doi.org/10.1016/j.jamcollsurg.2013.08.014. PubMed PMID: 24045144; PubMed Central PMCID: PMCPMC4106371.

1.9.9. Epithelial tumours of gallbladder and extrahepatic biliary tract (EBT)

1.9.9.1. Adenocarcinoma with variants of gallbladder

Wang H, Ling W, Luo Y. Contrast-enhanced ultrasound findings of gallbladder adenocarcinoma with sarcomatoid carcinoma accompanied by intrahepatic metastasis: A case report and literature review. Medicine (Baltimore). 2018;97(21):e10773. doi: https://doi.org/10.1097/MD.0000000000010773. PubMed PMID: 29794755.

Jurcic P. Dermatomyositis as the first manifestation of gallbladder adenocarcinoma: case report and literature overview. World J Surg Oncol. 2015;13:127. doi: https://doi.org/10.1186/s12957-015-0535-4. PubMed PMID: 25890241; PubMed Central PMCID: PMCPMC4379589.

Liu W, Wang L, He XD, Feng C, Chang XY, Lu ZH. Mixed large cell neuroendocrine carcinoma and adenocarcinoma of the gallbladder: a case report and brief review of the literature. World J Surg Oncol. 2015;13:114. doi: https://doi.org/10.1186/s12957-015-0533-6. PubMed PMID: 25890047; PubMed Central PMCID: PMCPMC4365805.

1.9.9.2. Adenocarcinoma with variants of EBT

Oliveira IS, Kilcoyne A, Everett JM, Mino-Kenudson M, Harisinghani MG, Ganesan K. Cholangiocarcinoma: classification, diagnosis, staging, imaging features, and management. Abdom Radiol (NY). 2017;42(6):1637-49. doi: https://doi.org/10.1007/s00261-017-1094-7. PubMed PMID: 28271275.

Mathema VB, Na-Bangchang K. Current insights on cholangiocarcinoma research: a brief review. Asian Pac J Cancer Prev. 2015;16(4):1307-13. PubMed PMID: 25743790.

Nakanuma Y, Kakuda Y. Pathologic classification of cholangiocarcinoma: New concepts. Best Pract Res Clin Gastroenterol. 2015;29(2):277-93. doi: https://doi.org/10.1016/j.bpg.2015.02.006. PubMed PMID: 25966428.

Voigtlander T, Lankisch TO. Endoscopic diagnosis of cholangiocarcinoma: From endoscopic retrograde cholangiography to bile proteomics. Best Pract Res Clin Gastroenterol. 2015;29(2):267-75. doi: https://doi.org/10.1016/j.bpg.2015.02.005. PubMed PMID: 25966427.

Vogel A, Wege H, Caca K, Nashan B, Neumann U. The diagnosis and treatment of cholangiocarcinoma. Dtsch Arztebl Int. 2014;111(44):748-54. doi: https://doi.org/10.3238/arztebl.2014.0748. PubMed PMID: 25412632; PubMed Central PMCID: PMCPMC4239580.

1.9.9.3. Squamous cell carcinoma of gallbladder and EBT

Kais H, Hershkovitz Y, Sandbank J, Halevy A. Port site metastases in squamous cell carcinoma of the gallbladder. Isr Med Assoc J. 2014;16(3):177-9. PubMed PMID: 24761709.

Domain 2.: Special web materials

The following links provide valuable, comprehensive informations and/or educational materials occasionally with clinico-pathological consequences about almost all cancer types including rare variants. Not only may they be useful for health care professionals and researchers, graduate students and postgraduate physician but also for patients and their caregivers or their relatives. Furthermore you may see the following books related to this topic, with well-formed illustration of the cancer types, about the macroscopy and their histological morphology. They also give information about the most important differential diagnosis, including the differencies between the common and rare variants as well. According to our experience in case of rare diseases (escpecially in cases of such malignancies) it's important to include them into the differential.

2.1. Links
http://www.pathologyoutlines.com/
http://www.webpathology.com
http://uscap.sclivelearningcenter.com/Index.aspx?PID=2870
http://knowledgehub.uscap.org/index.htm?hub.htm
http://apps.pathology.jhu.edu/sp/
http://www.uab.edu/medicine/pathology/education/cases

http://path.upmc.edu/casemonth/ap-casemonth.html
http://www.virtualpathology.leeds.ac.uk/cow/cow.php?year=2013
https://med.nyu.edu/pathology/caseoftheweek
https://medicine.hsc.wvu.edu/pathology/case-of-the-month/
https://www.oncolink.org/
https://www.cancer.gov/
http://www.cancerindex.org/

2.2. Books
Textbook of Uncommon Cancer, 5th Edition
Manual of Clinical Oncology, 7th Edition
Pediatric Oncology: A Comprehensive Guide, 3rd Edition
Lanzkowsky's Manual of Pediatric Hematology and Oncology, 6th Edition
Oncology Boards Flash Review, 1st Edition
New Trends in Cancer for the 21st Century, 1st Edition
Targeted Therapies for Solid Tumors: A Handbook for Moving Toward New Frontiers in Cancer Treatment
Successes and Limitations of Targeted Cancer Therapy
Melanoma: Translational Research and Emerging Therapies, 1st Edition
Cancer of the Head and Neck, 5th Edition
Series WHO:
WHO Classification of Tumours of Central Nervous System. Revised 4th edition
WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised Fourth Edition
WHO Classification of Tumours of the Digestive System. Fourth Edition
WHO Classification of Tumours of the Breast. Fourth Edition
WHO Classification of Tumours of Soft Tissue and Bone. Fourth Edition
WHO Classification of Tumours of Female Reproductive Organs. Fourth Edition
WHO Classification of Tumours of Lung Pleura, Thymus and Heart. Fourth edition
WHO Classification of Tumours of the Urinary System and Male Genital Organs. Fourth edition
WHO Classification of Head and Neck Tumours. Fourth edition
WHO Classification of Tumours of Endocrine Organs. Fourth Edition
Pathology and Genetics of Tumours of the Skin. Third edition
Series: Diagnostic Pathology
Diagnostic Pathology: Pediatric Neoplasms
Diagnostic Pathology: Endocrine
Diagnostic Pathology: Blood and Bone Marrow
Diagnostic Pathology: Lymph Nodes and Extranodal Lymphomas
Diagnostic Pathology: Bone
Diagnostic Pathology: Thoracic
Diagnostic Pathology: Hepatobiliary and Pancreas

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Diagnostic Pathology: Neoplastic Dermatopathology
Diagnostic Pathology: Genitourinary
Diagnostic Pathology: Head and Neck
Diagnostic Pathology: Neuropathology
Diagnostic Pathology: Breast
Diagnostic Pathology: Vascular
Diagnostic Pathology: Molecular Oncology
Diagnostic Pathology: Kidney Diseases
Diagnostic Pathology: Soft Tissue Tumors
Diagnostic Pathology: Gastrointestinal
Diagnostic Pathology: Gynecological
Diagnostic Pathology: Placenta
Diagnostic Pathology: Familial Cancer Syndromes

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Appendix 14

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS 2020/XX XX

Description of "Rare adult solid cancers" as a Medical Specialty in EU: Aims and objectives for specialist training

This specialty concerns the medical elements of diagnostic and care services provided to individuals and families, and sometimes populations with, or at risk of, conditions which have, or may have, a rare adult solid cancer basis. This includes the provision of diagnostic, counselling, and treatment services, information about the condition(s) and its implications, including management, prognosis, screening, preventionand reproductive options, and therapeutic possibilities. Provision of services is based on thorough clinical assessment, family medical information, conventional laboratory investigations and imaging, and specialized pathology tests. Other components of services include laboratory genetics (cytogenetics, molecular genetics, biochemical genetics, and genomics, including next generation techniques), specialized genetic counselling, and new techniques that are, or will, emerge from academic research. The core activities of the specialty can be defined as an integrated clinical and laboratory service, provided for those with, or who are concerned about, a disorder that may be a rare oncology disease. Sometimes, due to the sharing of genetic alleles among family members, the whole family, not only the individual, represents the core patient in this disease cohort. The current sketch uses the conditions, descriptions, terms, and recommendations summarized by the Joint Action on Rare Cancer (JARC) project that are found in the booklet entitled "Rare cancer Agenda 2030: 10 recommendations from the EU Joint Action on Rare Cancers; ISBN 978-88-31637-28-2."

Rare cancers can be defined as those malignancies whose incidence is <6/100,000/year. This definition is somewhat arbitrary, since there is no absolute frequency threshold that separates cancers, and diseases, into rare and common categories. Essentially, the definition was the product of a consensus process within the European oncology

community, funded by the EU RARECARE project, that took into account problems posed by rare cancers in terms of health care organization, clinical research, clinical decision-making (Gatta et al., EJC 2011). It is based on incidence, because unlike prevalence, incidence does not change depending on a factor different from frequency, such as expected survival time. As many diagnostic and therapeutic steps take place only once in the course of cancer development, incidence, unlike prevalence, is more fit to measure cancer burden. Using this threshold, one can draw up a list of rare cancers, that is useful for healthcare organizations, clinical research, and new therapy assessment and financing.

Any list of rare cancers needs to be derived from an established list of all cancers. The most obvious of these is the International Classification of Diseases for Oncology (ICD-O), which incorporates topographical and histological labels. The morphologic entities enlisted in the ICD-O need to be grouped into clinically distinct entities, which in turn may be gathered into families of neoplastic diseases, such as rare adult solid cancers. In 2007 within the RARECARE project, a panel of experts, including clinicians, pathologists and epidemiologists, agreed to build the first list of clinically relevant rare cancer entities on the basis of all the combinations of topography and morphologies coded in the ICD-O3. In 2017, the EU launched the JARC and a consensus effort to re-examine the list of rare cancers as developed by the RARECARE project took place within it, with a view also to rare cancers. In essence, the new list comprises three tiers. Tier 3 corresponds to the morphological entities of the ICD-O. Then, the experts were asked to group the ICD-O3 morphological entities, to give rise to a second tier of clinically distinct entitie by using morphologies and topographies (e.g., “squamous cell carcinoma of nasal cavity and sinuses”, “soft tissue sarcoma of limb”, etc.). These entities had to be viewed as clinically relevant by clinicians. In general, these entities had to correspond to consistent diagnostic and therapeutic approaches, so that, for example, they could be used as eligibility criteria in a clinical trial). Then, the Tier-2 entities were assembled into a smaller number of Tier-1 entities. These were intended to be major cancer entities in a clinical sense (e.g., “epithelial tumours of nasal cavity and sinuses”, “soft tissue sarcoma”) and to have an organizational importance: for example, they could underlie patient referral policies. Focusing on referral of patients, Tier-1 entities can be grouped into gross partitions, which give rise to what were called “families” of rare cancers, identifying major groups of rare cancers (e.g., “rare cancers of head & neck”, “sarcomas”, etc.). By and large, these are dealt with by the same disease-based communities of physicians and clinical

researchers. Tier-1 entities with an incidence rate <6/100,000/year define the major families of rare cancers (Table 1).

With regard to cancers in children and adolescents, the RARECARE list includes some of them under the family of "paediatric cancers", but several were included along with adult cancers in specific families, including haematological tumours, sarcomas, central nervous system tumours, head and neck cancers, digestive cancers, thoracic cancers, and endocrine tumours. All childhood cancers are rare, and should be considered as distinct from adult cancers affecting the same organs because their etiology is usually different. Furthermore, the risk of some cancers has a hereditary component. Some heritable cancers are rare cancers as such (e.g., sarcomas in Li Fraumeni syndrome), while others belong to common entities (e.g., colon adenocarcinoma in a familial adenomatous polyposis). Currently, there is no specific code for registration of heritable cancers as such, and some are considered among rare diseases.

An important challenge in medical education in rare diseases, including rare cancers, that makes it essentially different from common diseases is the lack of reinforcement of information. For example, when a physician attends an educational event on a common cancer, they will be likely to encounter patients with that cancer very soon and very often throughout their practice. The same does not apply when the cancer or disease is rare. Thus, the educational frame of any educational initiative in rare cancers must take this challenge into account. As to the current state of affairs, a survey was made on training programmes currently available for under- and postgraduates related to adult and paediatric cancers and is available on the website of JARC.

Ten recommendations from the EU Joint Action on Rare Cancers

The recommendations listed below were originally provided to all stakeholders involved in the rare adult solid cancer care, but they appear to be very useful when we depict the rare adult solid cancer general characteristics (from JARC booklet):

1. **Rare cancers are the rare diseases of oncology**

   and need specific approaches by the cancer community and by national health systems.

2. **Rare cancers should be strictly monitored**
epidemiologically and clinically, properly valuing population-based cancer registry data and real-world clinical data, favouring all efforts to merge data from all available data bases.

3. **Health systems should exploit networking**
around multidisciplinary centres of reference, to improve quality of care in rare cancers while diminishing/rationalizing health migration.

4. **Medical education should exploit and serve healthcare networking**
by proper integration of the university system, continuous medical education providers and all educational players, serving dedicated career mechanisms and opportunities for rare cancers.

5. **Research should be fostered by networking**
exploiting clinically annotated bio banking, clinical registering, patient referral to ongoing clinical studies.

6. **Patient-physician shared clinical decision-making should be especially valued**
being crucial to the appropriate approach to the possibly high degree of uncertainty posed by rare cancers.

7. **Appropriate state-of-the-art instruments should be developed in rare cancers**
fit to serve clinical decision-making in conditions of uncertainty.

8. **Regulatory mechanisms on rare cancers should properly face the challenge of a possibly higher degree of uncertainty**
being disease-adapted, opening up to innovative research methodologies, assuring certainty of rules to developers of innovation, recognizing enough flexibility as to allow a personalized clinical decision-making in conditions of uncertainty.

9. **Sustainability should be addressed by exploiting networking**
also providing evidence of its economies, and by pursuing a value-based medicine aware of the many difficulties of rare cancers.

10. Rare cancer patient advocates should be always involved

in all crucial areas, such as disease awareness and education, healthcare organization, state-of-the-art instruments, regulatory mechanisms, clinical and translational research, while having access to continuous education.

Special features: medical education and healthcare networking

In general, the medical education should be done by appropriate integration of the university system, continuous medical education providers, and all educational players, serving dedicated career mechanisms and opportunities for rare cancers. It also must be responsive to feedback from patient advocacy groups. In the rare adult solid cancer area patients very often remain without a specific doctor who takes charge of their treatment, which is an unsatisfactory situation.

Clearly, medical personnel of reference centres are a natural target of medical education on rare cancers, for reasons that do not differ substantially from the rationale for medical education on common cancers. However, by definition, rare cancers are scarce and there may be fewer opportunities for private sponsorships for events that focus on them, which means they will require more institutional support.

Medical personnel belonging to spokes of hub-and-spoke networks should be provided opportunities for medical education on rare cancers, since such personnel represent a target to develop, as long as hub-and-spoke networks spread. It is instrumental to the virtuous circle of quality improvement of spokes that such an education reaches out to their personnel. In fact, it is vital that clinicians within the spokes are able to collaborate effectively with hubs, in such a way as to virtually create the same kind of environment that exists within physically contiguous centres of reference. In other words, clinicians in spokes should be well aware of the diseases they are dealing with, even though their institutions do not see a number of cases comparable to hubs. For example, a medical oncologist in a spoke must be able to interact effectively with an experienced surgeon in a reference centre, in order to make medical therapy match all the needs of a planned highly specialized surgery. Of course, clinicians in spokes will not specialize only in one cancer amongst rare adult solid cancers, and these do not constitute a single set of cancers, unlike paediatric cancers, that are grouped together in the paediatric oncology area, and haematological cancers, that are grouped within the domain

of haemato-oncology. Thus, it is logical to conceive educational events that focus on several related rare adult solid cancers, (e.g., sarcomas and mesothelioma, etc.).

Undergraduates and general practitioners are a particularly challenging target, since the lack of information reinforcement is a major problem. However these providers are extremely important because the initial clinical diagnosis of a new suspect case will often rely on their degree of intuition and proper referral often depends on them. In general, it is important that non-oncologists perceive and importance of rare cancers and are aware of the main organizational challenges, of the importance of proper referral, of the meaning and the organization of clinical networking, of the difficulties of clinical research, and of the methodology of shared decision-making in conditions of uncertainty.

Given the crucial importance of these professional figures for networks, training opportunities should be arranged for case managers, patient navigators and other health professionals specializing in supporting networking functioning and the rare cancer patient journey.

The development of professional figures of nurses specializing in single rare cancers, within centres of reference, or some rare cancers, within rare cancer networks, should be encouraged and training facilities should be properly provided.

Medical education should be done through networking, as this approach will help shape and extend the contents of education on offer, while, obviously, it also allows IT facilities to convey tools for distance learning, distance mentorships, and the like. Distance learning may have the drawback of a lack of interaction between the mentor and the learner, but over a network this may be easily overcome by complementing distance tools with privileged connections between one teacher and one learner. Teleconsultation, within clinical networks, is obviously a healthcare resource that can improve quality of care in single cases, but it is also a powerful educational tool. After being teleconsulted, several clinical cases can then be grouped and offered as background educational material to the other members of the network, with a special view to young oncologists and other specialists.

Fellowships within networks are especially important. A clinical network is also based on personal relationships among clinicians, and even a relatively short fellowship at a centre of reference may not only mean a big opportunity for a young oncologist, but also a way to make sure that in the future two institutions may continue to work together. In other words, a fellowship at another institution of the network will mean much more. This is the reason why funding fellowships, even short fellowships, can be a powerful tool. Proper funding thereof should be guaranteed. It is important to realize that these fellowships may primarily have an

educational aim, even before a research one. Thus, EU funding should be arranged accordingly.

Long term, or even lifetime medical careers in rare adult solid cancers should be foreseen and should correspond to training pathways. Training on rare cancers should always be viewed as connected with available medical careers. An effort should be made to implement new medical careers focusing on rare cancers. Otherwise, rare cancer patients will be inevitably discriminated against. In that case young clinicians will not be attracted to work on these diseases, while professionals specializing in specific rare cancers at a given time of their career face the choice of keeping focused on them or losing their specialization to improve their positions. In other words, it is vital that medical careers are fully developed on rare cancers, to make sure that professionals can spend their entire professional lives being dedicated to rare cancers. At the same time, these medical careers need relevant training pathways. Clearly, reference centres have developed careers on rare cancers, though with difficulties to avoid escapes of professionals to more attractive positions elsewhere. Centres belonging to ERNs should be the first to guarantee medical careers on rare cancers. Now, it would be important to develop careers also in the spokes of the hub-and-spoke networks on rare cancers.

Dedicated institutions do exist in the paediatric oncology area, and also in the haemato-oncology area, therefore with dedicated full medical careers. However, these areas do not belong to the current specialty. Contrary, institutions and units dedicated exclusively to rare adult solid cancers are scarce or lacking, while there may exist institutions or units dedicated to one or few rare adult solid cancers. Medical oncology units dedicated to rare adult solid cancers should be created within spokes of hub-and-spoke networks on rare cancers, with full careers. Any specific training is lacking. A clinical oncologist specializing in rare adult solid cancers (or some of them) is likely already a medical oncologist, a radiation oncologist, or a surgical oncologist. Thus, there is the need to provide educational pathways for clinical oncologists willing to specialize on rare adult solid cancers. These educational pathways should provide education on such diseases under a multidisciplinary perspective. They should be flexible enough to accommodate educational needs that may cover all or only some of the 10 families or rare adult solid cancers. These educational pathways could be provided in collaboration with the universities linked to EURACAN, during or after the conventional board certification pathway (i.e., in medical oncology, radiation oncology, surgical oncology). These pathways should include: a) courses on each of the rare adult solid cancers, based on a syllabus; b) clinical fellowships on selected rare adult solid cancers. There

should be an examination, with a certification of competence. All this could give rise to an integrated system leading to the creation of experts on rare adult solid cancers, hopefully finding dedicated careers for them at the centres of hub-and-spoke networks.

Taken together, at the moment exclusively a new UEMS examination and qualification system may serve as the provider of the certification and the European training requirements. This may serve later a base for the ERNs private and dedicated systems, and for future national qualification systems as well.

Table 1.
Rare cancers: RARECARE "families" and "Tier-1" entities with an incidence <6/100,000

HEAD & NECK
Epithelial tumours of the larynx
Epithelial tumours of the hypopharynx
Epithelial tumours of the nasal cavity and sinuses
Epithelial tumours of the nasopharynx
Epithelial tumours of major salivary glands and salivary-gland type tumours
Epithelial tumours of the oropharynx
Epithelial tumours of the oral cavity and lip
Epithelial tumours of the eye and adnexa
Epithelial tumours of the middle ear

DIGESTIVE
Epithelial tumours of the small intestine
Epithelial tumours of the anal canal
Epithelial tumours of the gallbladder and extrahepatic biliary duct

THORACIC
Epithelial tumours of the trachea
Thymomas and thymic carcinomas
Malignant mesothelioma

FEMALE GENITAL
Non-epithelial tumours of the ovary
Epithelial tumours of the vulva and vagina
Trophoblastic tumours of the placenta

MALE GENITAL & UROGENITAL
Tumours of the testis and paratestis
Epithelial tumours of penis
Extragonadal germ cell tumours
Epithelial tumours of renal pelvis, ureter and urethra

SKIN CANCERS - Rare & **NON CUTANEOUS MELANOMA**
Mucosal melanoma
Uveal melanoma
Adnexal skin carcinomas
Kaposi sarcoma

SARCOMAS
Soft tissue sarcoma
Bone sarcoma
Gastrointestinal stromal tumours

NEUROENDOCRINE (NET)
NET GEP
NET lung
NET other sites

ENDOCRINE ORGAN cancers
Thyroid cancers
Parathyroid cancer
Adrenal cortex cancer
Pituitary gland cancer

CENTRAL NERVOUS SYSTEM (CNS) tumors
Glial tumours and others**
Malignant meningioma
Embryonal tumours of CNS

#PEDIATRIC CANCERS*
Hepatoblastoma
Neuroblastoma & ganglioneuroblastoma
Nephroblastoma
Odontogenic malignant tumours
Olfactory neuroblastoma
Pancreatoblastoma
Pleuropulmonary blastoma
Retinoblastoma

#HEMATOLOGICAL
Lymphoid malignancies**
Myelodysplastic syndromes
Myeloproliferative neoplasms (including mastocytosis)
Myelodysplastic/myeloproliferative neoplasms
Myeloid/ lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2
Acute myeloid leukaemia and related neoplasms

#Neither the Paediatric, nor the hematological rare diseases belong to this specialty; here we did not delete them from the original classification to help the reader to be able to understand the full classification as it was described in the JARC.
* Other neoplasms which mainly, or also, occur in childhood are included under other labels (e.g., Ewing's sarcoma and osteosarcoma under bone sarcomas; rhabdomyosarcoma under soft tissue sarcoma; medulloblastoma under embryonal tumor of CNS)
** All subgroups (Tier-2 entities) within are rare

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif International non-profit organisation

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu

T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

Training Requirements for the Specialty of

Rare Adult Solid Cancers

Preamble

The UEMS is a European-level non-governmental organisation representing national associations of medical specialists. With a current membership of 39 national associations and operating through 43 Specialist Sections and European Boards, the UEMS is committed to promoting the free movement of medical specialists across Europe while ensuring the highest level of training. Its work promises to pave the way to improved quality of care for the benefit of all European citizens. The UEMS areas of expertise notably encompass Continuing Medical Education, Post Graduate Training and Quality Assurance.

It is the UEMS' conviction that the quality of medical care and expertise is directly linked to the quality of training provided to medical professionals. Therefore the UEMS has committed itself to contributing to the improvement of medical training at the European level through the development of European standards in the different medical disciplines. No matter where doctors are trained, they should have at least the same core competencies. This is also essential for enabling free movement of medical specialists.

In 1994, the UEMS adopted its Charter on Post Graduate Training, which provided recommendations for good medical training throughout Europe. Made up of six chapters, this Charter set the basis for the European approach in the field of Post Graduate Training. The first five chapters established guidelines common to all specialties, while Chapter 6 was to be completed by each Specialist Section according to the specific needs of the discipline.

For more than a decade after the introduction of this Charter, the UEMS Specialist Sections and European Boards have continued to work on developing European standards in medical training that reflects modern medical practice and current scientific findings. In doing so, the UEMS Specialist Sections and European Boards do not aim to supersede the prerogatives of national authorities to define the content of postgraduate training in their own states, but rather to complement them and ensure that high quality training is provided across Europe.

At the European level, the legal mechanism ensuring the free movement of doctors through the recognition of their qualifications was established in the 1970s by the European Union. Sectorial Directives were adopted and one Directive addressed specifically the issue of medical training at the European level. However, in 2005, the European Commission proposed to the European Parliament and Council to have a unique legal framework for the recognition of professional qualifications to

facilitate and improve the mobility of all workers throughout Europe. This Directive, 2005/36/EC, established the mechanism of automatic mutual recognition of qualifications for medical doctors according to training requirements within all Member States; this is based on the length of training in the Specialty and the title of qualification.

Given the long-standing experience of UEMS Specialist Sections and European Boards on the one hand and the European legal framework enabling Medical Specialists and Trainees to move from one country to another on the other hand, the UEMS is uniquely in position to provide specialty-based recommendations. The UEMS values professional competence as "*the habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values, and reflection in daily practice for the benefit of the individual and community being served*"[1]. While professional activity is regulated by national law in EU Member States, UEMS understands that it has to comply with international treaties and UN Declarations on Human Rights as well as the WMA International Code of Medical Ethics.

This document derives from the previous Chapter 6 of the Training Charter and provides definitions of specialist competencies and procedures as well as how to document and assess them. For the sake of transparency and coherence, it has been renamed as "Training Requirements for the Specialty of Rare Adult Solid Cancers". This document aims to provide the basic Training Requirements for each specialty and it should be regularly updated by UEMS Specialist Sections and European Boards to reflect scientific and medical progress. Its three-part structure reflects the UEMS approach to have a coherent pragmatic document not only for medical specialists but also for decision-makers at national and European levels interested in knowing more about medical specialist training.

Rare adult solid cancers are a broad and diverse group of cancers with a wide range of survival outcomes. Rare adult solid cancers are defined by the European Union as malignancies with an incidence of less than 0.006%. Using incidence in this definition elucidates the difference between rare adult solid cancers with high cure rates and relatively common cancers with low cure rates. A rare adult solid cancer that is successfully cured has a rather high prevalence rate (such as testicular cancer) while a common cancer such as small-cell lung cancer has a low life-expectancy and hence a low prevalence in the population. It is estimated that there are 198 types of rare adult solid cancer. Some of these are unusual types of common cancers such as versions of bowel and breast cancer, while others are completely separate kind such as several sarcomas.

The public health challenge posed by rare adult solid cancers combines both the typical problems of rare diseases (such as limited relevant professional expertise available in the community, or the difficulties in clinical research) and those of cancer, with the need of a timely and appropriate diagnosis and optimal treatment from the very beginning of the patient's journey. An accurate clinical, pathologic and biological assessment of the disease of the individual patient, as well as an expert and prompt clinical decision provided by a multidisciplinary team, is key to survival and cure.

[1] Defining and Assessing Professional Competence, Dr Ronald M. Epstein and Dr Edward M. Houndert, Journal of American Medical Association, January 9, 2002, Vol 287 No 2

Rare Adult Solid Cancer Training Aims (more details in the Description of Specialty and the Syllabus)

A competent rare adult solid cancer specialist needs knowledge of the underlying disease processes, available diagnostic and therapeutic modalities, and also must appreciate the importance of epidemiology and the potential for prevention of these cancers. Rare adult solid cancer specialists who generally work in hospitals need as well to integrate their work with community based primary care colleagues and other hospital based physicians. The training requirements for the specialty of rare adult solid cancers described below will ensure these competencies.

1. To provide a service whose goal is to assess, investigate, and diagnose rare adult solid cancers and medical conditions
2. To provide a service that provides specialist information about rare adult solid cancers, including recommendations for screening where appropriate
3. To provide a service that investigates and offers counselling in relation to reproductive options and prenatal genetics, balancing the goal of preventing hereditary rare adult solid cancers with the personal choices of the individuals and families affected.
4. To contribute to the management and treatment of patients and families affected by rare adult solid cancers, in collaboration with other medical specialists
5. To be advocates, where necessary, for those affected by rare adult solid cancers
6. To conduct and contribute to clinical and genomic research aimed at improving knowledge of the causation and natural history of rare adult solid cancers and conditions
7. To teach and instruct medical undergraduates and postgraduates in rare adult solid cancers, in order to raise the knowledge base across all medical specialties
8. To provide a knowledge and skills resource to all medical specialties, including through multidisciplinary meetings
9. To contribute to public awareness about rare adult solid cancers

I. TRAINING REQUIREMENTS FOR TRAINEES

1. Content of training and learning outcome

The rare adult solid cancers speciality is a field of medicine concerned with the investigation, diagnosis, treatment, prevention, and research into rare adult solid cancers. The scope of patient care activities includes the recognition of rare adult solid cancers, the early identification of individuals and families at risk, the identification of possible causative genetic defects and the preventive care of affected family members, and prevention of intellectual and physical disability in those born with genetic disorders, in addition to the rehabilitation of such patients. This specialty training is aimed at giving doctors appropriate qualifications in the field of rare adult solid cancers to enable them to treat patients and their families in the light of current and expanding knowledge on the subject, with particular emphasis on understanding the molecular and cellular pathogenic mechanisms of such diseases, and their diagnosis and treatment. Rare adult solid cancer specialists must also be able to carry out screening for the early identification of individuals and families with a high risk of contracting common diseases that have a major social impact (malformations in general, familial cancers, inborn errors of metabolism, etc.).

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Fields of rare adult solid cancers :

1. Head and neck cancers
1.1. Epithelial tumours of nasal cavity and sinuses
    1.1.1. Squamous cell carcinoma with variants of nasal cavity and sinuses
    1.1.2. Lymphoepithelial carcinoma of nasal cavity and sinuses
    1.1.3. Undifferentiated carcinoma of nasal cavity and sinuses
    1.1.4. Intestinal type adenocarcinoma of nasal cavity and sinuses
1.2. Epithelial tumours of nasopharynx
    1.2.1. Squamous cell carcinoma with variants of nasopharynx
    1.2.2. Papillary adenocarcinoma of nasopharynx
1.3. Epithelial tumours of major salivary glands and salivary-gland type tumours
    1.3.1. Epithelial tumours of major salivary glands
    1.3.2. Salivary gland type tumours of head and neck
1.4. Epithelial tumours of hypopharynx and larynx
    1.4.1. Squamous cell carcinoma with variants of hypopharynx
    1.4.2. Squamous cell carcinoma with variants of larynx
1.5. Epithelial tumours of oropharynx
    1.5.1. Squamous cell carcinoma with variants of oropharynx
1.6. Epithelial tumours of oral cavity and lip
    1.6.1. Squamous cell carcinoma with variants of oral cavity
    1.6.2. Squamous cell carcinoma with variants of lip
1.7. Epithelial tumours of eye and adnexa
    1.7.1. Squamous cell carcinoma with variants of eye and adnexa
    1.7.2. Adenocarcinoma with variants of eye and adnexa
1.8. Epithelial tumours of middle ear
    1.8.1. Squamous cell carcinoma with variants middle ear
    1.8.2. Adenocarcinoma with variants of middle ear
2. Thoracic rare cancers
2.1. Epithelial tumour of trachea
    2.1.1. Squamous cell carcinoma with variants of trachea
    2.1.2. Adenocarcinoma with variants of trachea
    2.1.3. Salivary gland type tumours of trachea
2.2. Rare epithelial tumours of lung
    2.2.1. Adenosquamous carcinoma of lung
    2.2.2. Large cell carcinoma of lung
    2.2.3. Salivary gland type tumours of lung
    2.2.4. Sarcomatoid carcinoma of lung
2.3. Epithelial tumours of thymus
    2.3.1. Malignant thymoma
    2.3.2. Squamous cell carcinoma of thymus
    2.3.3. Undifferentiated carcinoma of thymus
    2.3.4. Lymphoepithelial carcinoma of thymus
    2.3.5. Adenocarcinoma with variants of thymus
2.4. Malignant mesothelioma
    2.4.1. Mesothelioma of pleura and pericardium

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

2.4.2. Mesothelioma of peritoneum and tunica vaginalis
3. Male genital and urogenital rare cancers
3.1. Rare epithelial tumours of prostate
3.1.1. Squamous cell carcinoma with variants of prostate
3.1.2. Infiltrating duct carcinoma of prostate
3.1.3. Transitional cell carcinoma of prostate
3.1.4. Salivary gland type tumours of prostate
3.2. Testicular and paratesticular cancers
3.2.1. Paratesticular adenocarcinoma with variants
3.2.2. Non seminomatous testicular cancer
3.2.3. Seminomatous testicular cancer
3.2.4. Spermatocytic seminoma
3.2.5. Teratoma with malignant transformation
3.2.6. Testicular sex cord cancer
3.3. Epithelial tumours of penis
3.3.1. Squamous cell carcinoma with variants of penis
3.3.2. Adenocarcinoma with variants of penis
3.4. Rare epithelial tumours of kidney
3.4.1. Squamous cell carcinoma spindle cell type of kidney
3.4.2. Squamous cell carcinoma with variants of kidney
3.5. Epithelial tumours of pelvis and ureter
3.5.1. Transitional cell carcinoma of pelvis and ureter
3.5.2. Squamous cell carcinoma with variants of pelvis and ureter
3.5.3. Adenocarcinoma with variants of pelvis and ureter
3.6. Epithelial tumours of urethra
3.6.1. Transitional cell carcinoma of urethra
3.6.2. Squamous cell carcinoma with variants of urethra
3.6.3. Adenocarcinoma with variants of urethra
3.7. Rare epithelial tumours of bladder
3.7.1. Squamous cell carcinoma with variants of bladder
3.7.2. Adenocarcinoma with variants of bladder
3.7.3. Salivary gland type tumours of bladder
3.8. Extragonadal germ cell tumours
3.8.1. Non seminomatous germ cell tumours
3.8.2. Seminomatous germ cell tumors
3.8.3. Germ cell tumors of central nervous system (CNS)
4. Female genital rare cancers
4.1. Rare epithelial tumours of breast
4.1.1. Mammary paget's disease of breast
4.1.2. Special types of adenocarcinoma of breast
4.1.3. Metaplastic carcinoma of breast
4.1.4. Salivary gland type tumours of breast
4.1.5. Epithelial tumour of male breast
4.2. Rare epithelial tumours of corpus uteri
4.2.1. Squamous cell carcinoma with variants of corpus uteri
4.2.2. Adenoid cystic carcinoma of corpus uteri

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

4.2.3. Clear cell adenocarcinoma not otherwise specified (NOS) of corpus uteri
4.2.4. Serous (papillary) carcinoma of corpus uteri
4.2.5. Mullerian mixed tumour of corpus uteri
4.3. Epithelial tumours of cervix uteri
4.3.1. Squamous cell carcinoma with variants of cervix uteri
4.3.2. Adenocarcinoma with variants of cervix uteri
4.3.3. Undifferentiated carcinoma of cervix uteri
4.3.4. Mullerian mixed tumour of cervix uteri
4.4. Epithelial tumours of ovary and falloppian tube
4.4.1. Adenocarcinoma with variants of ovary
4.4.2. Mucinous adenocarcinoma of ovary
4.4.3. Clear cell adenocarcinoma of ovary
4.4.4. Primary peritoneal serous/papillary carcinoma of ovary
4.4.5. Mullerian mixed tumour of ovary
4.4.6. Adenocarcinoma with variant of falloppian tube
4.5. Non epithelial tumours of ovary
4.5.1. Sex cord tumours of ovary
4.5.2. Malignant/immature teratomas of ovary
4.5.3. Germ cell tumour of ovary
4.6. Epithelial tumours of vulva and vagina
4.6.1. Squamous cell carcinoma with variants of vulva and vagina
4.6.2. Adenocarcinoma with variants of vulva and vagina
4.6.3. Paget s disease of vulva and vagina
4.6.4.Undifferentiated carcinoma of vulva and vagina
4.7. Trophoblastic tumour of placenta
5. Neuroendocrine tumours
5.1. Rare neuroendocrine tumours
5.1.1. GEP - well differentiated not functing endocrine carcinoma of pancreas and digestive system
5.1.2. GEP - well differentiated functing endocrine carcinoma of pancreas and digestive system
5.1.3. GEP - poorly differentiated endocrine carcinoma of pancreas and digestive system
5.1.4. GEP - mixed endocrine-exocrine carcinoma of pancreas and digestive system
5.1.5. Endocrine carcinoma of thyroid gland
5.1.6. Rare neuroendocrine carcinoma of skin
5.1.7. Typical and atypical carcinoid of the lung
5.1.8. Rare neuroendocrine carcinoma of other sites
5.1.9. Pheochromocytoma malignant
5.1.10. Paraganglioma
6. Tumours of the endocrine organs
6.1. Carcinomas of pituitary gland
6.2. Carcinomas of thyroid gland
6.3. Carcinomas of parathyroid glan
6.4. Carcinoma of adrenal gland
7. CNS tumours
7.1. Tumours of central nervous system (CNS)

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

- 7.1.1. Astrocytic tumours of CNS
- 7.1.2. Oligodendroglial tumours of CNS
- 7.1.3. Ependymal tumours of CNS
- 7.1.4 Choroid plexus carcinoma of CNS
- 7.1.5. Malignant meningiomas

7.2. Embryonal tumours of central nervous system (CNS)
8. Sarcomas
8.1. Soft tissue sarcoma

- 8.1.1. Soft tissue sarcoma of head and neck
- 8.1.2. Soft tissue sarcoma of limbs
- 8.1.3. Soft tissue sarcoma of superficial trunk
- 8.1.4. Soft tissue sarcoma of mediastinum
- 8.1.5. Soft tissue sarcoma of heart
- 8.1.6. Soft tissue sarcoma of breast
- 8.1.7. Soft tissue sarcoma of uterus
- 8.1.8. Other soft tissue sarcomas of genitourinary tract
- 8.1.9. Soft tissue sarcoma of viscera
- 8.1.10. Soft tissue sarcoma of paratestis
- 8.1.11. Soft tissue sarcoma of retroperitoneum and peritoneum
- 8.1.12. Soft tissue sarcoma of pelvis
- 8.1.13. Soft tissue sarcoma of skin
- 8.1.14. Soft tissue sarcoma of paraorbit
- 8.1.15. Soft tissue sarcoma of brain and other parts of nervous system
- 8.1.16. Embryonal rhabdomyosarcoma of soft tissue
- 8.1.17. Alveolar rhabdomyosarcoma of soft tissue
- 8.1.18. Ewin's sarcoma of soft tissue

8.2. Bone sarcoma

- 8.2.1. Osteogenic sarcoma
- 8.2.2. Chondrogenic sarcomas
- 8.2.3. Notochordal sarcomas chordoma
- 8.2.4. Vascular sarcomas
- 8.2.5. Ewing's sarcoma
- 8.2.6. Epithelial tumours adamantinoma
- 8.2.7. Other high grade sarcomas (fibrosarcoma malignant fibrous histiocytoma)

8.3. Gastrointestinal stromal sarcoma
9. Digestive rare cancers
9.1. Epithelial tumours of oesophagus

- 9.1.1. Squamous cell carcinoma with variants of oesophagus
- 9.1.2. Adenocarcinoma with variants of oesophagus
- 9.1.3. Salivary gland type tumours of oesophagus
- 9.1.4. Undifferentiated carcinoma of oesophagus

9.2. Rare epithelial tumours of stomach

- 9.2.1. Squamous cell carcinoma with variants of stomach
- 9.2.2. Salivary gland-type tumours of stomach
- 9.2.3. Undifferentiated carcinoma of stomach

9.3. Epithelial tumours of small intestine
- 9.3.1. Adenocarcinoma with variants of small intestine
- 9.3.2. Squamous cell carcinoma with variants of small intestine

9.4. Rare epithelial tumours of colon
- 9.4.1. Squamous cell carcinoma with variants of colon
- 9.4.2. Fibromixoma and low grade mucinous adenocarcinoma of the appendix

9.5. Rare epithelial tumours of rectum
- 9.5.1. Squamous cell carcinoma with variants of rectum

9.6. Epithelial tumours of anal canal
- 9.6.1. Squamous cell carcinoma with variants of anal canal
- 9.6.2. Adenocarcinoma with variants of anal canal
- 9.6.3. Paget's disease of anal canal

9.7. Rare epithelial tumours of pancras
- 9.7.1. Squamous cell carcinoma with variants of pancreas
- 9.7.2. Acinar cell carcinoma of pancreas
- 9.7.3. Mucinous cystadenocarcinoma of pancreas
- 9.7.4. Intraductal papillary mucinous carcinoma invasive of pancreas
- 9.7.5. Solid pseudopapillary carcinoma of pancreas
- 9.7.6. Serous cystadenocarcinoma of pancreas
- 9.7.7. Carcinoma with osteoclast-like giant cells of pancreas

9.8. Epithelial tumours of liver and intrahepatic bile tract (IBT)
- 9.8.1. Hepatocellular carcinoma of liver and IBT
- 9.8.2. Hepatocellular carcinoma fibrolamellar of liver and IBT
- 9.8.3. Cholangiocarcinoma of IBT
- 9.8.4. Adenocarcinoma with variants of liver and IBT
- 9.8.5. Undifferentiated carcinoma of liver and IBT
- 9.8.6. Squamous cell carcinoma with variants of liver and IBT
- 9.8.7. Bile duct cystadenocarcinoma of IBT

9.9. Epithelial tumours of gallbladder and extrahepatic biliary tract (EBT)
- 9.9.1. Adenocarcinoma with variants of gallbladder
- 9.9.2. Adenocarcinoma with variants of EBT
- 9.9.3. Squamous cell carcinoma of gallbladder and EBT

Competencies required of the trainee

Rare adult solid cancer specialist need a wide range of clinical skills, as rare cancers can affect all body systems.

A holistic vision of patients and good communication skills are particularly important for the trainee.

2. Organization of training

a. Schedule of training

A medical trainee (intern, resident, fellow or registrar) is a doctor who has completed their general professional training as a physician and is in an accredited training programme to become a recognised medical specialist. The trainee in rare adult solid cancer must be recognized as a trainee according to the regulations in force in each EU/EEA member state. The duration and curriculum of

training in rare adult solid cancers should enable the trainee to become a fully independent specialist. The optimal rare adult solid cancer speciality training is 4 years consisting of 1 year of common trunk and 3 years training in an accredited program in a rare adult solid cancer centre.

b. Training curriculum

The general aim of the training program is to enable the rare adult solid cancer specialist to work effectively as a consultant. The trainee must demonstrate the ability to record and convey patient details of history, examination, and investigation findings to senior staff. The trainee must communicate effectively with patients and relatives, and be able to pass on both technical information in a way that it can be received with understanding, and distressing information in a sensitive and caring manner.

c. Assessment and evaluation

The MJC RUD aims to introduce an EU Board Exam in Rare Adult Solid Cancers. The successful candidates will gain an European Certificate in Rare Adult Solid Cancers (ECRASC), which is intended to be the main knowledge-based assessment tool for training and assessment across Europe and ultimately for all continent's experts, with the aim of establishing world class-leading standards in that specialty throughout all countries. At the moment, there is no such national level exam anywhere in Europe. Later, countries may use their own assessment strategies appropriate to their needs, provided they introduce their own training and assessment systems. Knowledge will be assessed through a form of examination. This examination would use scenarios from an agreed list of core clinical conditions and test knowledge in the areas of relevant science and clinical practice (diagnosis, investigation, interpretation, prevention and treatment). Whether the examination will be written or oral in nature, and its precise format, remains to be determined.

The ECRASC examination will be jointly developed by the UEMS Multidisciplinary Joint Committee (UEMS-MJC RUD) and the sections, MJCs, and national medical associations. European scientific societies, world networks, like the former Joint Action Rare Cancers (JARC) members, and the Undiagnosed Disease Network International (UDNI) are also expected to join this effort. The examination will be overseen and supervised by the Examination Steering Committee. It will be open to candidates who are trainees or fully trained experts from any nation. The ECRASC will be an excellence exam, and will be valid for practice only in countries where it is ratified as an official certificate for this purpose by national regulatory bodies or organisations.

Continuous medical education (CME) and continuous professional development (CPD) to keep updated with developments in diagnosis and management of rare adult cancer conditions as well as of global professional skills are obligations of the accredited expert. Type, duration, content and monitoring of CME/CPD activity will fall under the authority of national boards that need to be established, and these boards should consider the general recommendations of the UEMS. The UEMS provides European accreditation of CME (EACCME) for international events according to defined quality standards. It is recommended that trainees in rare adult solid cancer field are introduced to CME/CPD during their postgraduate training period.

d. Governance
Governance of each training program will be the responsibility of the Program or Course Director and the institution(s) in which the training program is being delivered. A trainer (who will have satisfied the requirements laid out below, Section II) will be responsible to the Program Director for delivering the required training in their area of practice.

II. TRAINING REQUIREMENTS FOR TRAINERS

1. Process for recognition as trainer

a. Requested qualification and experience
Trainers should be certified rare adult solid cancer specialists and must be recognized by the national authority. Trainers should provide evidence of academic activities (clinical and/or basic research, publications in peer reviewed journals and participation in clinical genetic scientific meetings) and professional experience. They should possess the necessary administrative, communicative, teaching and clinical skills and commitment to conduct the program. Trainers and Training Program Directors must be in active clinical practice and engaged in training in the training center. A Training Program Director must be a certified specialist for a minimum of 5 years. He/she organizes the activities of the educational program in all institutions that participate in the program.

b. Core competencies for trainers
1. Familiar with all aspects of rare adult solid cancers
2. Experienced in teaching and in supporting learners
3. Trained in the principles and practice of medical education
4. Lectures to a peer-audience on a regular basis, attends national meetings and is able to demonstrate appropriate participation in continuing professional development
5. Able to recognize trainers whose professional behavior is unsatisfactory and to initiate corrective and supportive measures as needed

2. Quality management for trainers
Trainers and Program Directors will have their job descriptions agreed with their employer, which will allow them sufficient time for support of trainees. Feedback from trainees is necessary for optimal training. The educational work of trainers and Program Directors will be appraised no less than on an annual basis within their institution as local circumstances determines.

III. TRAINING REQUIREMENTS FOR TRAINING INSTITUTIONS

1. Process for recognition as training center

a. Requirement on staff and clinical activities
A training center is a place, or number of places, where trainees are able to develop their competences in rare adult solid cancers. Thus, training may take place in a single institution, or in a network of institutions working together, to provide training in the full spectrum of clinical conditions and skills detailed in the curriculum. A training institution must have national accreditation, in agreement with UEMS standards, and should possess an adequate infrastructure and offer

qualitative and quantitative clinical exposure. Optimally, they are member(s) of one or more European Reference Networks (ERNs).

Each participating institution in a network must be individually recognized as a provider of a defined section of the curriculum. Training centers must have a sufficient throughput of patients, an appropriate case-mix to meet training objectives, and be adequately resourced with teaching staff.

The training must expose the trainee to a broad range of clinical experience. The training of a trainee will be led and managed by a specialist. This specialist will be active in the practice, with personal responsibility for the management of patients with a wide range of rare adult solid cancers. Within a training center there should be a team of specialists, each with subspecialty expertise and able to supervise and train a trainee. Allied specialties must be present to a sufficient extent to provide the trainee with the opportunity of developing his/her skills in a multidisciplinary approach to patient care. There is no specific trainee/trainer ratio required, but there should be a minimum of two trainers in a training center, and it is likely that non-medical healthcare professionals will also be engaged.

The trainee should be involved in the diagnosis and management process of new patients (outpatients and in-patients), as well as their follow up. A trainee must demonstrate personal responsibility for the global care of patients with rare adult solid cancers. There should be written general guidelines within the training institution concerning patient care and patient information (including informed consent), referrals, medical records, documentation, on-call and back-up schedules, attendance at conferences and educational/training courses.

The staff of a training center should engage collaboratively in regular reviews and audit of the center's clinical activity and performance. There should be regular multi-disciplinary meetings to determine optimal care for patients, involving both medical and other healthcare professionals.

Specialist staff appointed to a training center will have completed all training requirements themselves and will have been trained also in teaching and mentoring trainee staff, staff as well as in working in a multidisciplinary team with lab and genetic counsellors.

b. Requirement on equipment, accommodation

A training center should have sufficient equipment and support to enable the clinical practice that would be expected of a training center and thus provide the necessary educational opportunities for trainees. The trainee must have adequate time and opportunities for practical and theoretical study and have access to adequate professional literature. Computing, Information Technology and library resources must be available. All trainees must engage in clinical audit and have the opportunity to engage in research.

2. Quality Management within Training Institutions
Participation of the training institution in a certified quality management program with an external auditing process on a regular basis is consistent with good governance. Criteria of quality management at specialty training institutions include the following:

Accreditation
Training institutions need to be accredited with competent National Medical Boards. Additional accreditation on a supra-national level, such as that provided by some professional societies, and in an European Board, is strongly recommended. A training institution must have an internal system of medical audit or quality assurance. Quality assurance must be an integral part of the training program of all training institutions and networks. A national register of approved institutions and networks should be available. Internal regulations: There should be written general guidelines within the training institution concerning patient care and patient information (including informed consent), referrals, medical records, documentation, leave (annual, study, maternity/paternity), residents' working schedules, conference attendance and educational activities. These should be available to staff and trainees.

Clinical governance
Employee structure at training institutions needs to be designed in a way to accommodate for specialty training. Workload has to be managed with a priority on training.

Manpower planning
Training institutions should appoint a coordinator responsible for the composition, implementation and supervision of a specialty training program. Roles of trainer and trainee need to be clearly defined. Allotted time of at least one day per workweek should be implemented for specialty training interaction. Manpower planning is under the jurisdiction of each member state according to their needs for rare adult solid cancer specialists.

Regular report
Annual reports on various aspects of an institution's specialty training program should be made publically available.

External audit
Training institutions should appoint a coordinator who is also responsible for compliance of the training program with current guidelines, directives or regulations of competent medical boards, as well as the local medical school.

Transparency of training programs
Based on national and regional guidelines, UEMS strongly encourages training institutions to formulate defined training programs and make them publicly available, for example, on their website. It would be expected that a training center would publish details of the training provision available with details of the clinical service it provides and the names of the trainers. Such information would include the training programs, the nature of the clinical or laboratory experiences in which a trainee would be engaged, and the support and interaction with the trainer and Program Director. There would be a named individual whom a prospective trainee might contact and discuss the program.

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

Framework of approval
As part of training programs it should also be made clear how and by whom key achievements of training will be ascertained, leading the trainee to a higher level of clinical responsibility and new assignments. To assist a European medical specialist with additional clinical competence moving from one EU country to another it would be expected that they have satisfactorily completed a training program. After the examination in rare adult solid cancers they may be able to demonstrate that they have the required knowledge, clinical and laboratory skills and competences, as well as having demonstrated appropriate professional behaviors. Such accomplishments would be verified both by relevant documents and by the testimony of trainers and other staff who have worked with the trainee.

Feedback from trainers and trainees
Feedback about program quality from both trainers and trainees must be systematically sought, analyzed and acted upon. Trainers and trainees should be actively involved in using its results for program improvement and development.

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif *International non-profit organisation*
RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS 2020/xxx

European Training Requirements for "Neuroendocrine Neoplasia Medicine"

European Standards of Postgraduate Medical Specialist Training

Preamble

The UEMS is a non-governmental organization representing national associations of medical specialists at the European Level. With a current membership of 34 national associations and operating through 39 Specialist Sections and European Boards, the UEMS is committed to promote the free movement of medical specialists across Europe while ensuring the highest level of training which will pave the way to the improvement of quality of care for the benefit of all European citizens. The UEMS areas of expertise notably encompass Continuing Medical Education, Post Graduate Training and Quality Assurance. It is the UEMS' conviction that the quality of medical care and expertise is directly linked to the quality of training provided to the medical professionals. Therefore, the UEMS committed itself to contribute to the improvement of medical training at the European level through the development of European Standards in the different medical disciplines. No matter where doctors are trained, they should have at least the same core competencies. In 1994, the UEMS adopted its Charter on Post Graduate Training aiming at providing the recommendations at the European level for good medical training. Made up of six chapters, this Charter set the basis for the European approach in the field of Post Graduate Training. With five chapters being common to all specialties, this Charter provided a sixth chapter, known as "Chapter 6", that each Specialist Section was to complete according to the specific needs of their discipline. More than a decade after the introduction of this Charter, the UEMS Specialist Sections and European Boards have continued working on developing these European Standards in Medical training that reflects modern medical practice and current scientific findings.
In doing so, the UEMS Specialist Sections and European Boards did not aimed to supersede the National Authorities' competence in defining the content of postgraduate training in their own State but rather to complement these and ensure that high quality training is provided across Europe. At the European level, the legal mechanism ensuring the free movement of doctors through the recognition of their qualifications was established back in the 1970s by the European Union. Sectorial Directives were adopted, and one Directive addressed specifically the issue of medical Training at the European level. However, in 2005, the European Commission proposed to the European Parliament

and Council to have a unique legal framework for the recognition of the Professional Qualifications to facilitate and improve the mobility of all workers throughout Europe. This Directive 2005/36/EC established the mechanism of automatic mutual recognition of qualifications for medical doctors according to training requirements within all Member States; this is based on the length of training in the Specialty and the title of qualification. Given the long-standing experience of UEMS Specialist Sections and European Boards on the one hand and the European legal framework enabling Medical Specialists and Trainees to move from one country to another on the other hand, the UEMS is uniquely in position to provide specialty-based recommendations. The UEMS values professional competence as "the habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values, and reflection in daily practice for the benefit of the individual and community being served". While professional activity is regulated by national law in EU Member States, it is the UEMS understanding that it must comply with International treaties and UN declarations on Human Rights as well as the WMA International Code of Medical Ethics. This document derives from the previous Chapter 6 of the Training Charter and provides definitions of specialist competencies and procedures as well as how to document and assess them. For the sake of transparency and coherence, it has been renamed as "Training Requirements for the Specialty of X". This document aims to provide the basic Training Requirements for each specialty and should be regularly updated by UEMS Specialist Sections and European Boards (ENETS) to reflect scientific and medical progress. The three-part structure of this documents reflects the UEMS approach to have a coherent pragmatic document not only for medical specialists but also for decision-makers at the National and European level interested in knowing more about medical specialist training.

This document supports the role of UEMS in setting Standards in the field of PGT, ref to Charter on PGT. It was approved by the UEMS Specialist Section and the European Neuroendocrine Tumor Society at the UEMS Council meeting on 25 April, 2020. This Document is designed to harmonize training programs in Neuroendocrine Neoplasia Medicine between different European countries.

Introduction

In 2004, the European Neuroendocrine Tumor Society (ENETS) was founded by a group of European medical specialists in the field of neuroendocrine neoplasia. The society members, currently numbering nearly 1,200, bring a variety of expertise from such fields as oncology, surgery, pathology, radiology, nuclear medicine, endocrinology, and gastroenterology to ENETS. The main goal of the society since then has been to integrate basic and clinical research with teaching and to establish guidelines for the diagnosis and therapy of gastro-entero-pancreatic neuroendocrine neoplasia (NEN). A further role of ENETS is to critically appraise the available evidence and therewith facilitate the transfer of knowledge to the clinicians and advise these clinicians on the best treatment for their patients.

In 2018 - 2019, as an initiative of ENETS that two of the ENETS Advisory Board members, Andrea Frilling and Andreas Pascher, the General Secretary of the UEMS, Vasilios Papalois, and the President of Multidisciplinary Joint Committee (MJC) of Rare and Undiagnosed Diseases (RUD) of UEMS, Bela Melegh, signed a MoU, then meet in London, UK. According to the general UEMS viewpoints about the Multidisciplinary Joint Committees, a primary aim of them is to certify the highest standards of education for physicians and other learners in order to promote patient safety, they aim to advance the science of clinical education, training, and assessment in a multidisciplinary manner in sections with mutual interest on the field of the MJC. The MJC aims to create a system of support for the delivery of state-of-the-art clinical skills training within the European Union (EU) and EU affiliated countries in the UEMS area. The ENETS and the MJC RUD collaborated then is development of this ETR.

I. Training requirements for trainees

Curriculum

Requirements for training:

- Medical profession
- Fellowship or equivalent in specialty
- Log Book
- ENETS membership
- Clinical training:

- Minimum of 2 years of continuous clinical work in NEN care after fellowship in ENETS Centers of Excellence or equivalent institution according to the training requirements for training institutions (see III.)
- Regular active participation in dedicated NEN tumor boards (minimum number of 100; as to be proven in log book)
- Active involvement in design and conduction of therapeutic pathways according to individual specialty (minimum number of 50; as to be proven in log book)

Requirements for application for examination:

- ENETS member in good standing
- Recommendation by trainer
- Completed and signed log book
- Participation in one postgraduate course per year (@ENETS congress)

- Attendance at national NE symposium / registry meeting
- Participation or organization of at least one educational event for NEN patients or awareness campaign
- Successful attendance at ENETS-E-Learning platform
- Minimum of 3 (co-)authorships in peer-reviewed publications in the field of NEN disease during the last 5 years
- Minimum of 2 oral or poster presentations on NEN disease at national or international symposia/congresses

Syllabus

Pathology – diagnosis and prognostic stratification

Gross analysis and processing of tissues
Diagnostic standards
    Neuroendocrine phenotype
        Mandatory and optional elements for assessing a biopsy/specimen
Differentiation
    WHO and UICC/AJCC classifications
    Grading
    Mandatory elements for assessing a tum our with features of a GEP NEN
    Optional diagnostic markers (e.g. immunostaining for hormones, somatostatin receptors, serotonin or CDX2))
Minimum requirements of pathology reports
Predictive markers of a response to treatment (e.g. MGMT)
Knowledge of molecular markers

Endocrinology- diagnosis and treatment

Knowledge of neuroendocrine phenotype
    Sporadic, hereditary, hereditary syndromes
    Functional and non-functional NEN
    Ectopic hormonal syndrome

Endocrine emergencies
Establishing of a diagnosis of NEN
    Biochemical diagnosis
    Standard tumor markers
    Differential diagnoses
    Stimulations tests for diagnosis and primary tumor localization

Search for a primary tumor
Treatment of symptoms induced by hormonal hyper- and hyposecretion
Somatostatin analogues
Treatment of symptoms induced by hormonal hyposecretion

Imaging – morphologic imaging and functional imaging

US, CT, MRI
Specific imaging aspects of pancreas NEN
Specific imaging aspects of small bowel NEN and their loco-regional disease
Specific imaging aspects of neuroendocrine liver metastases
Somatostatin receptor based functional imaging
Octreoscan, ^{68}Ga DOTA-PET/CTs,^{68}Ga DOTA-Exendin-4 PET/CT
Non- Somatostatin receptor based functional imaging
^{18}F FDG PET/CT, ^{18}F DOPA PET/CT
Pitfalls in morphologic and functional imaging

Interventional radiology

Diagnostic imaging guided biopsy
Percutaneous organ directed treatment (pancreas, liver)
Ablation (e.g. RFA, microwave, laser)
Transarterial embolization (e.g. TAE, TACE, SIRT)
Techniques of blood sampling for hormonal essays and tumor localization
Emergency interventions (e.g. embolization)

Gastroenterology- diagnosis and treatment

Causes of diarrhea in NEN patients
Differential diagnosis of hypergastrinemia
Differential diagnosis of jaundice
Differential diagnosis of ascites
Knowledge in nutrition
Diagnosis and treatment of malnutrition and weight loss
Understanding of disease-related digestive and metabolic dysfunction
Indications for diagnostic upper GI endoscopy and colonoscopy
Endoscopic techniques
Endoscopy, ultrasound guided biopsy, endoscopic ultrasound, video capsule endoscopy, balloon enteroscopy
Endoscopic tumor ablation (e.g. EMR, ESD, FTRD)

Stenting
Treatment of hormonally induced gastro-intestinal symptoms
Treatment of carcinoid syndrome
Treatment of pancreatic insufficiency
Treatment of short bowel syndrome
Treatment of emergency conditions (e.g bleeding, bile leak)

Pre- and Peri-operative / Peri-interventional Management

Assessment of the tumor type and hormone production
Carcinoid syndrome
- Definition
- Preoperative fluid, electrolyte, vitamin, and protein abnormalities
- Carcinoid heart disease
- Carcinoid crisis
- Atypical carcinoid syndrome
- Specific recommendations concerning anaesthesia
- Perioperative treatment with Octreotide

Pancreatico-duodenal NEN
- Gastrinoma, Zollinger-Ellison syndrome
  - e.g. PPIs
- Insulinoma
  - e.g. Diazoxid
- Glucagonoma
- VIPoma

Syndromes related to ectopic hormonal secretion
- Hypercortisolism
- Hypersecretion of PTH

Surgery

Selection of patients for surgical treatment
Gastric NEN – Indication for surgery and surgical strategy
Duodenal NEN - Indication for surgery and surgical strategy
Pancreatic NEN- Indication for surgery and surgical strategy
- Sporadic NEN, MEN1 associated NEN
- Functioning and non-functioning NEN
- Small (<2cm) non-functioning NEN
- Surgical complications and their management

Small bowel NEN – Indication for surgery and surgical strategy

- Specific aspects of resection of loco-regional (mesenteric) lymph node metastases
- Surgical complications and their management

Colonic NEN- Indication for surgery and surgical strategy
Appendix NEN – Surgical strategy
- Goblet cell cancer- Surgical strategy

Rectal NEN- Indication for surgery and surgical strategy
Neuroendocrine liver metastases - Indication for surgery and surgical strategy
- Resection (R0/R1)
- Principles of debulking (R2)
- Risks of liver surgery and management of complications

Liver transplantation – Patient selection, principles of transplantation medicine, surgical strategy
Neoadjuvant and adjuvant treatment concepts
Resection of the primary tumor in the presences of non-resectable distant metastases

Systemic therapy

Patient selection
Mechanisms of action, indications, contraindications, dosing, side-effects
Targeted therapy
- Somatostatin analogues
- Everolimus
- Sunitinib
- Peptide receptor radionuclide therapy with radiolabelled somatostatin analogues
  - ^{90}Y PRRT, ^{177}Lu PRRT
  - Specific aspects- selection of patients, side-effects, kidney protection
  - Knowledge of principles of theranostics

Interferon-Alpha
Chemotherapy (e.g. STZ/5-FU, temozolamide/capecitabine, platinum-based regimens for poorly differentiated grade 3 NEC, oxaliplatin- or irinotecane-based regimes)
Immunotherapy
Telotristat
Assessment, grading and reporting of side-effects of systemic therapy
Knowledge of major trials in the field of NEN
Principles of follow-up of NEN patients

Radiotherapy

Indications in NEN patients (e.g. bone metastases, brain metastases)

Palliative treatment and supportive care

Indications, principles

Primary tumor specific aspects of diagnosis and management of NEN

Appendix NEN
- Goblet cell carcinoma
- MANEN

Gastric NEN
Duodenal NEN
Pancreatic NEN
- Functioning
- Non-functioning
  - Sporadic NEN
  - Hereditary NEN
    - Hereditary syndromes (e.g. MEN 1 syndrome)

Primary hepato-biliary NEN
Small bowel NEN
Colonic NEN
Rectal NEN
Cancer of unknown primary tumor origin (CUP NEN)

Special knowledge

Holistic needs of NEN patients
Quality of life assessment in NEN patients
Patient reported outcomes of treatment
Multidisciplinary management of NEN patients
Cooperation with patient advocacy groups
Structure of a NEN center of excellence / NEN specialized centers
Current unmet needs and future developments in NEN field

Competences required

Life-long learning and reflective thinking; critical reading and appraisal of up-dated information relevant to neuroendocrine neoplasia as well as inpatient and ambulatory medicine
Acquisition of basic tools for teaching (including supervision), skills for research and education presentations, teaching of young colleagues, residents and allied healthcare professionals
Effective, open empathic and respectful communication with patients and family/relatives
Effective and professional communication with colleagues and other collaborators to ensure optimal patient care
Multidisciplinary and inter-professional team working in acute care, as well as in the context of protocol implementation
Effective communication in the setting of multidisciplinary teams in the resolution of conflicts, decision-making skills, giving feed-back, taking and assuming leadership
Implementation and use of quality assurance programs according to recognized national and international standards
Implementation and use of local, national and international practice guidelines and standards while complying with national healthcare policies
Promotion of and participation in better and safer patient care
Knowledge of administrative, medico-legal, ethical, and economical aspects, as well as inpatient and outpatient management principles
Contribution to research, development, and implementation of new medical knowledge as well as auditing
Contribution to education of patients, students and healthcare professionals

II. Training requirements for trainers

- ENETS member
- UEMS certified specialist in Neuroendocrine Neoplasia Medicine (desirable)
- Continuous supervision of clinical training
- Signs Log book
- Takes UEMS examinations
- Approved application as trainer by ENETS Executive Committee

UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif – International non-profit organisation

III. Training requirements for training institutions

ENETS Centres of Excellence
Institutions with expertise and infrastructure comparable with ENETS Centres of Excellence as to be approved by ENETS

Recommended readings: ENETS Guidelines, available on www.enets.org

Version 31/01/2020
Drafted by Andrea Frilling and Andreas Pascher

RUE DE L'INDUSTRIE, 24
BE- 1040 BRUSSELS
www.uems.eu
T +32 2 649 51 64
F +32 2 640 37 30
info@uems.eu

UEMS - EUROPEAN UNION OF MEDICAL SPECIALISTS

MULTIDISCIPLINARY JOINT COMMITTEE ON RARE AND UNDIAGNOSED DISEASES

Annual Report of the President – 2019

10 February, 2020

The calendar year of 2019 was the third full year in the history of the MJC RUD.

Membership

We had a total of 39 members from 11 Sections (OMF, IM, Ophthalmology, Paediatrics, Psychiatry, Rheumatology, Medical Genetics, Neurology, Paediatric Surgery, Pharmacology, and Rehabilitation. They represented 21 Countries, and of them 3 were non EU Nations (Armenia, Georgia, Turkey). The following NMAs have delegates: Austria, Georgia, Greece, Spain, The Netherlands, Turkey.

The Bureau

There was an electronic vote organized by the Coordination; Pr. Alessandra Renieri was elected as Secretary, and Serdar Ceylander as vice President. The Bureau consisted of the President, Secretary, and a vice President.

Meetings

There was no official membership meeting during the year. However, both the President and the Secretary participated at the London UEMS Council Meeting, and there was a non-official gathering of the participating MJC RUD members.

Main focus in 2019 and after

Construction of ETR of Rare and Undiagnosed Diseases, Rare Adult Solid Cancer, and the ENETS ETR.

Finances

During the year of 2019 there was still no independent budget of the MJC RUD. However, the president evaluated 5 life events for the CESMA.

Participation in other activities

The president participated in the work of the CESMA (talk at the Barcelona meeting), and continued with the EACCME "Training the reviewers" working group. There was a meeting with the ENETS representatives.

Béla Melegh
President