Number 12 Spring 2013

European Society of Pathology

Pathology newsletter

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Word from the President Prof. F. Carneiro

Since the last Newsletter (Winter 2012) an intense activity has been developed by the ESP in different fronts.

One of the major actions was the revision of the ESP Statutes and Bylaws, in order to acknowledge the new management model and to fulfill the aims and current challenges of the Society. The ESP lawyer and accountant played a crucial role during this quite long process. The revised Statutes and Bylaws will be made available to the ESP members who will be invited to provide suggestions and comments for improvement. This is indeed a major issue and I would like to stress that we need your collaboration from now until September 4, 2013. This is the date of the General Assembly, the body that has the sole authority to change the Statutes and Bylaws. For that purpose a massive attendance of the next General Assembly (during the Lisbon Congress) is required and the ESP counts on the mobilization of its members to achieve this goal. The new version of the Statutes, translated to Dutch language, will be published in the Belgian Official Gazette ("Bijlagen bij het Belgisch Staatsblad"), to conform to provisions of Belgian law.

The Executive Committee has been engaged in the nomination and electoral process for the offices of President-elect and Secretary and the four new Executive Committee members. The procedure has followed the current Statutes and Bylaws. In this Newsletter you will find the recommendations of the Executive Committee for the aforementioned positions as well as an invitation for other nominations.

The initiative on International Collaboration on Cancer Reporting (ICCR) acknowledged the request of the ESP to work with the ICCR on common datasets, to be included in the expert groups and to have representation on the writing committees. In the future, when the ICCR embarks on a dataset of a new organ site, a member of the relevant ESP WG will be included in the expert group. European pathologists will now join those of the USA, Canada, Australia and the UK as partners in this international collaborative effort and the ESP will provide an ESP nominee on the ICCR organizing committee.

The preparation of the Lisbon Congress (August 31 – September 4) is quite advanced. The preliminary programme was published and distributed to all ESP members and is available at the Congress website (www.esp-congress.org). The scientific activities will be centered upon Diagnosis, Prognosis and Prediction, having Personalized Pathology as the ultimate goal. Following the *motto* of the Congress – "Pathology – A gate to the future" – a particular attention has been paid to the Residents who will organize, among other scientific and social activities, a Plenary Residents Seminar whose "Grande Finale" will take place at the closing events of the Congress. For the purpose of the Plenary Residents Seminar (PRS), 12 leading Departments of Pathology from Portugal were invited to submit 2 cases each, that will be available online every month from January to June 2013 (4 cases each month). From the 24

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cases, 4 will be selected by Prof. Ales Ryska to be presented at the Congress by the Residents. To make this initiative as lively as possible, all Pathologists and Residents are invited to observe and discuss the cases, make comments and propose diagnoses. To have access to the cases you just have to connect to http://prs.slidesci.org/ and follow the simple instructions displayed on screen.

The preparation of the 26th ECP is moving smoothly, in a joint organization of the ESP and the Pathological Society of Great Britain & Ireland. This Congress will be held in London, from 30 August to 3 September 2014. Future Congresses approved by the last General Assembly of the ESP will be held in Belgrade (2015) and Cologne (2016), the latter jointly organized by the ESP and the German Division of the IAP. Proposals from the ESP Executive Committee for the venues for ECP 2017 (Amsterdam) and ECP 2018 (Bilbao) will be presented in the next General Assembly (during the Lisbon Congress).

The Education Committee has been deeply involved in the process of building the Education Portal, to be opened (hopefully) before the Lisbon Congress.

A very fruitful meeting on external quality assurance (EQA) in molecular pathology was held in Naples, March 22-23, 2013. The action plan derived from this meeting encompasses several initiatives, including the proposal to create a European database for EQA schemes in molecular pathology.

Looking forward to the Lisbon Congress, the ESP invites all of you to visit the Congress website (www.esp-congress.org).

It will be a pleasure to welcome you in Lisbon!

Fátima Carneiro

www.esp-congress.org

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LISBON CONGRESS

Concert at São Carlos National Theatre

performed by the Coro Gulbenkian (conducted by Jorge Matta)

Programme Summary

(for further details please visit the website of Lisbon Congress: http://www.esp-congress.org)

The program opens up a panoramic soundscape, even though still partial, onto the musical life ongoing in Portugal and Brazil between the middle of the 17th century and the early years of the 19th century and in two very particular contexts. The first is that of the official sacred music played at the great liturgical festivals of the Patriarchal Church of Lisbon and so very often in the presence of the royal court alongside other senior political and ecclesiastical dignitaries from the reign of King João V onwards. This model would naturally bear repercussions on the musical repertoire performed in the main cathedrals across Brazil throughout the colonial period by Portuguese and Brazilian chapel masters with prominent maestros including André da Silva Gomes, in São Paulo, and José Maurício Nunes Garcia, in Rio de Janeiro. These ostentatious religious ceremonies frequently had the royal court of King João VI in attendance after 1808 following its relocation to Brazil due to the vicissitudes of history.

The second specific context evoked is the sacred repertoire of the black or Creole Villancicos deriving from the Augustine monks of the Santa Cruz Monastery of Coimbra in the mid-17th century. Among the monastery's residents, there were a number of highly talented musicians and composers with high levels of education given that the majority were from aristocratic backgrounds. They produced this interesting set of sacred musical works composed for the liturgical celebration of Christmas and distinctively theatrical in nature and with a strong festive dimension. One particularly curious facet of this repertoire is its incorporation of a series of linguistic characteristics, rhythms and lyrics from different ethnic backgrounds – especially from Portugal's African colonies – that had been interweaving with the Portuguese social reality ever since the 16th century. This musical repertoire, with every indication that it was produced within the church context, very suggestively illustrates the cultural interchange that had gradually taken root in daily interactions and relationships ongoing between persons from different ethnic backgrounds within the context of the pluri-continental Portuguese monarchy towards the end of the Ancien Régime.

Mariana Portas

São Carlos National Theatre

São Carlos National Theatre

Gulbenkian Corus

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Election of Officers of the European Society of Pathology

At the General Assembly in Lisbon in September 2013, the following officers will demit office:

President-elect Prof. Han van Krieken (as from September 2013 **President of the ESP)**

Secretary Prof. Ilmo Leivo (Prof. Leivo has expressed his willingness to continue his work as Secretary for another four years)

The ESP Executive Committee:

Prof. Aurelio Ariza
Prof. Jean Francois Fléjou
Prof. Janina Kulka
Prof. Arzu Ensari
Prof. Generoso Bevilacqua
Prof. Silvana Di Palma
Prof. Laurence de Leval
Prof. Hans Kreipe

recommends these individuals for the following positions:

*President elect with effect from September 2013:

Prof. Pierre Bedossa (Paris, France)

*Secretary with effect from September 2013

Prof. Ilmo Leivo (Turku, Finland)

Their brief CVs are available on request.

The membership is now invited to make other nominations within six weeks of this communication. Any nomination must be approved by the individuals themselves and each must be supported by at least 5% of the members of the society and accompanied by an abbreviated CV of no more than one page.

Prof. Fatima Carneiro

ESP President

Election of Four New Members of the Executive Committee of the ESP.

At the General Assembly in Lisbon in September 2013, the following four members of the Executive Committee will demit office:

Prof. Generoso Bevilacqua
Prof. Silvana Di Palma
Prof. Laurence de Leval
Prof. Hans Kreipe

The following individuals are recommended by the Executive Committee to fill these positions:

Prof. Holger Moch (Switzerland)
Prof. Ales Ryska (Czech Republic)
Prof. Dina Tiniakos (Greece)
Prof. Gordan Vujanic (UK)

Their brief CVs are available on request.

These recommended candidates will be presented for formal approval at the General Assembly in Lisbon in September 2013.

Prof. Fatima Carneiro

ESP President

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In Illo Tempore

This photo (Fig.1) was taken at the Norwegian Radium Hospital, Oslo, in March 1985, during the meeting of the Scientific Committee of the X European Congress of Pathology (ECP) that would be held in Athens, Sept 1-6, 1985.

This meeting was held one year after the Joint meeting of the Executive Committee of the European Society of Pathology (ESP) and the Scientific Committee of the X ECP (Fig. 2) also at the Norwegian Radium Hospital, Oslo, on March 10, 1984.

Prof. Jan Vincents Johannessen (1) was the President and Prof. Sture Falkmer the Secretary of the ESP.

The most important point of the agenda of the Joint meeting (1984) was the forthcoming Athens Congress: The President, the late Prof. N. Papacharalampous (2), the Chairman of the Local Organising Committee (LOC), the late Prof. George Tiniakos (3) and the General Secretary, Prof. Niki Agnantis (4) gave a detailed description of the on-going organization. It was decided that the early registration fee would be "USD 200 for members of the European Society of Pathology and USD 220 for non-members. After June 1, 1985, the fee will be USD 220 and USD 250, respectively". It was also decided that "Because of the present difficult situation as regards the possibility to obtain foreign currency, the participants from the East-European countries may be exempted from paying the registration fee".

The Executive Committee decided also that "At the X Congress in Athens, honorary membership will be given to Profs Groniowski, Nezelof and Piringer-Kuchinka. On the same occasion, Prof. Hedinger will be nominated for honorary membership at the XI Congress in Prague, 1987".

The sequence of the ESP Presidents in this period was the following: Prof. J. V. Johannessen was the President of the Society in the Athens Congress (1985), Prof. G. Seifert (5) in the Prague Congress (1987) and Prof. A. Llombart-Bosch (6) in the Porto Congress (1989). Prof. D. Ferluga (7), who had been ESP President in the Hamburg Congress (1983), proposed Ljubljana as site for the 1991 ECP that was eventually cancelled due to the regional war. Prof. D. Ferluga organized later on, in 2003, a superb Congress in Ljubljana, Slovenia (XIX ECP).

The other gentlemen in the picture are Prof. D. Williams (8), Prof. G. Coggi (9), Prof. D. Serrão (10) and Prof. A. Hecht (11).

The links with the forthcoming Lisbon Congress – XXV ECP (August 31-Sept 4, 2013)

Professor Daniel Serrão had suggested Lisbon as the XII ECP (1989) but the Executive Committee decided it would be better to hold it in Porto, having Prof.Antonio Llombart-Bosch as ESP President, Prof. Daniel Serrão as Congress President and Manuel Sobrinho-Simões as Chairman of the LOC. Fátima Carneiro had just got her Specialist degree and has been one of the driving forces of the LOC of the XII ECP. One of the Plenary Sessions of the Lisbon Congress will commemorate the 150th anniversary of the creation of the Academic Chairs of Pathology in Coimbra, Lisbon and Porto, having Prof. Daniel Serrão as Guest Speaker and Prof. Antonio Llombart-Bosch as Chairperson.

Fifty years ago (March 30, 1963), Prof. Giordano chaired, in Brussels, the Foundation Meeting of the ESP. The meeting was attended by Prof. Scarff (UK), Prof. Mellgren (Sweeden), Prof. Orcel (France), Prof. Krauspe (West Germany), Prof. Schornagel (The Netherlands) and, as representatives of the "Société Belge d' Anatomie Pathologique", Prof. Maisin, Prof. Dustin and Prof. Betz. At the Lisbon Congress we will commemorate the 50th anniversary of the ESP founding event in a Plenary Session chaired by Prof. D. Ferluga and having Prof. J.V. Johannessen as Guest Speaker.

Dina Tiniakos, daughter of Prof. George Tiniakos, will organise together with Anna Batistatou an art exhibition – "Art Paths in Lisbon" – that will be held at the Lisbon Congress (for details, please visit the website: http://esp-pathology.org).

All the former Presidents and Officers of the ESP have been invited to attend the XXV ECP and it would be a privilege to host them in Lisbon. Besides the ESP personalities who have been in charge of the ESP activities in the XXI century, we hope to have in Lisbon Prof. C. Nezelof, Prof. S. Falkmer, Prof. G. Seifert, Prof. U. van Haelst and Christine van Haelst, Prof. C. Berry, Prof. G. Coggi, Prof. J.M. Nesland, Prof. R. Heimann and Prof. G. Klöppel.

Porto, March 25, 2013

Fátima Carneiro Manuel Sobrinho-Simões

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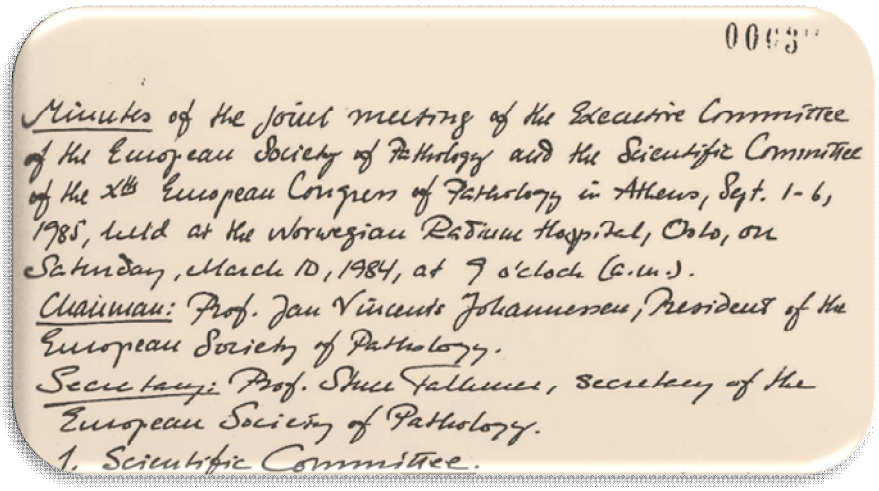
Legends:

Fig.1 – Members of the Scientific Committee of the X European Congress of Pathology (ECP), in the Norwegian Radium Hospital, Oslo, March 1985.

Fig. 2 – Minutes of the Joint meeting of the Executive Committee of the European Society of Pathology (ESP) and the Scientific Committee of the X European Congress of Pathology (ECP). Oslo, March 1984



0063

Minutes of the joint meeting of the Executive Committee of the European Society of Pathology and the Scientific Committee of the xth European Congress of Pathology in Athens, Sept. 1-6, 1985, held at the Norwegian Radium Hospital, Oslo, on Saturday, March 10, 1984, at 9 o'clock (a.m.).

Chairman: Prof. Jan Vincents Johannessen, President of the European Society of Pathology.

Secretary: Prof. Stein Gallefoss, secretary of the European Society of Pathology.

1. Scientific Committee.

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The Quality assurance program on KRAS testing of the ESP: ongoing progress.

Prof. Han van Krieken

The number of molecular tests, we as pathologists perform for treatment decisions increases rapidly. As we all know, these new tests need a different approach to validation and external quality assurance (EQA) and it is therefore that the ESP had decided to set up a European program for EQA for KRAS mutational analysis in colorectal cancer. This program was set up with emphasis on the close interaction of pathologists and molecular biologists under the guidance of Els Dequeker, who is very experienced in quality assurance for molecular tests. The set-up of the program was supported by Amgen. The outline and early results of this program has been described earlier in the newsletter, was published in Virchows Archive (and is well received: 123 citations within 4 years), and the Oncologist.

More than 300 laboratories participated so far and those with a good result can be found via the ESP website. Next to KRAS mutation testing for patients with colorectal cancer, ALK and EGFR testing has become the topic of external quality assurance. This first round was completed in 2012 and the second is ongoing, with Eric Thunnissen as coordinator.

Important developments have taken place and through the quality assurance program we learned a lot. We know now that each round about 10-15% laboratories have not a good enough result. We have learned that we are able to indicate laboratories that are not good enough, and also that then can improve based on our feedback. We know that for colorectal cancer and KRAS testing the primary tumor is reliable and there is no need to take a biopsy from a metastasis. The crucial issue of number of tumor cells in a sample, the problems with sensitivity in case there are few has become very apparent. The value and problems of artificial slides in quality assurance have become clear. Finally, recently a document was published in Virchows archive which gives a guideline for the organization of quality assurance program in molecular pathology.

There are nevertheless still quite some challenges. Next generation sequencing is rapidly replacing standard methods and the number of genes that need to be evaluated in a certain tumor is increasing. These two developments go along together very well, but it is extremely difficult to create reliable quality assurance for such approaches. In March 22nd-23rd, the 2nd meeting on quality assurance in molecular pathology took place in Naples, organized by Nicola Normanno, and this was one of the major topics.

It is the vision of the ESP that molecular pathology is now an integrated part of pathology and thus it is important high quality can be delivered. Where possible the ESP wishes to support this vision. Much more information can be found on the website.

Han van Krieken

References:

1: van Krieken JH, Normanno N, Blackhall F, Boone E, Botti G, Carneiro F, Celikl, Ciardiello F, Cree IA, Deans ZC, Edsjö A, Groenen PJ, Kamarainen O, Kreipe HH,Ligtenberg MJ, Marchetti A, Murray S, Opdam FJ, Patterson SD, Patton S, Pinto C,
Rouleau E, Schuuring E, Sterck S, Taron M, Tejpar S, Timens W, Thunnissen E, van de Ven PM, Siebers AG, Dequeker E. Guideline on the requirements of external quality assessment programs in molecular pathology. Virchows Arch. 2013;462:27-37.

2: Dijkstra JR, Heideman DA, Meijer GA, Boers JE, 't Hart NA, Diebold J,Hirschmann A, Hoefler G, Winter G, Miltenberger-Miltenyi G, Pereira SV, Richman SD, Quirke P, Rouleau EL, Guinebretiere JM, Tejpar S, Biesmans B, van Krieken JH.
KRAS mutation analysis on low percentage of colon cancer cells: the importance of quality assurance. Virchows Arch. 2013;462:39-46.

3: Dijkstra JR, Opdam FJ, Boonyaratanakornkit J, Schönbrunner ER, Shahbazian M,
Edsjö A, Hoefler G, Jung A, Kotsinas A, Gorgoulis VG, López-Ríos F, de Stricker K, Rouleau E, Biesmans B, van Krieken JH. Implementation of formalin-fixed, paraffin-embedded cell line pellets as high-quality process controls in quality assessment programs for KRAS mutation analysis. J Mol Diagn. 2012;14:187-91.

4: Dequeker E, Ligtenberg MJ, Vander Borght S, van Krieken JH. Mutation analysis of KRAS prior to targeted therapy in colorectal cancer: development and evaluation of quality by a European external quality assessment scheme. Virchows Arch. 2011;459:155-60.

5: Bellon E, Ligtenberg MJ, Tejpar S, Cox K, de Hertogh G, de Stricker K, Edsjö A, Gorgoulis V, Höfler G, Jung A, Kotsinas A, Laurent-Puig P, López-Ríos F, Hansen TP, Rouleau E, Vandenberghe P, van Krieken JJ, Dequeker E. External
quality assessment for KRAS testing is needed: setup of a European program and report of the first joined regional quality assessment rounds. Oncologist. 2011;16:467-78.

6: Knijn N, Mekenkamp LJ, Klomp M, Vink-Börger ME, Tol J, Teerenstra S, Meijer JW, Tebar M, Riemersma S, van Krieken JH, Punt CJ, Nagtegaal ID. KRAS mutation analysis: a comparison between primary tumours and matched liver metastases in
305 colorectal cancer patients. Br J Cancer. 2011;104:1020-6.

7: van Krieken JH, Jung A, Kirchner T, Carneiro F, Seruca R, Bosman FT, Quirke P, Fléjou JF, Plato Hansen T, de Hertogh G, Jares P, Langner C, Hoefler G, Ligtenberg M, Tiniakos D, Tejpar S, Bevilacqua G, Ensari A. KRAS mutation testing for predicting response to anti-EGFR therapy for colorectal carcinoma: proposal for an European quality assurance program. Virchows Arch. 2008;453:417-31.

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QA Meeting on Molecular Pathology 22nd-23rd March 2013, Naples

Report of Krasi Serguieva

On 22nd-23rd March 2013 in Naples, the second meeting on quality assurance on molecular pathology took place. The event was sponsored by the ESP, AIOM and SIAPEC. Almost thirty people attended the meeting representing academia, pharma, and industries. The event was chaired by Prof. Van Krieken from the ESP and Prof. Normanno from the AIOM.

During the meeting many topics were discussed and series of actions were planned. Task forces were created to deal with the important points listed below:

- There is a need for formal recognition of the present group/initiative by European agencies and/or accreditation bodies.
- There is need for a guideline on reporting based on existing documents like the ISO norm, the CAP guideline and others
- There is need for recognition of clinical molecular biologists in pathology/clinical scientist in molecular pathology by the ESP
- The ESP is advised to create a label for EQA programs in molecular pathology
- There is good progress in the creation of a database with results of EQA schemes. This project will move on with support of the ESP
- EQA programs for FISH for ALK alterations and Her2 amplifications are already being developed/executed. For diagnostic tests for lymphoma and sarcoma there is an unmet need.
- The need for a guideline on criteria for laboratories that perform molecular tests was recognised and will be addressed
- It is very clear that a need for EQA for platforms/NGS approaches is going to be needed soon. A group will create the first ideas

The group will meet again in September this year during the European Congress of Pathology of the ESP in Lisbon in order to report on the developments of the above-described action points.

It was felt that more parties should be invited to participate in the future QA in molecular pathology meetings, such as: patients, statisticiens, and regulators.

Next year 2014, the group will meet again in Naples as it is considered a perfect meeting location and the event was organized smoothly by AIOM represented locally by Prof. Nicola Normanno. Most important, the meeting was very successful with many decisions and actions derived of a great importance for the future of molecular pathology.

Gynaecological Pathology WG of the ESP

Report by Dr. Maria Raspollini

Dear Colleagues,

I am glad to summarize the recent activities of the Gynaecological Pathology Working Group in 2012 and to inform about the future activities of the Group.

During last year, major effort was given to prepare the guidelines on tumour sampling and reporting of ovarian surface epithelial/stromal tumours. After a systematic review of published studies, the analysis of WHO classification, and of FIGO staging, the guidelines, drafted by myself and Dr. Lynn Hirschowitz (Birmingham, UK), were revised by six distinguished experts of our group namely Harry Hollema; Sigurd Lax; Glenn McCluggage; Francisco Nogales; Jaime Prat; and Michael Wells. These guidelines have been presented during the business meeting of our Group at the 24th European Congress of Pathology held in Prague on September 2012 and endorsed by the group members and ultimately presented to the ESP Executive Board. These guidelines represent a tentative to homogenize the pathologists' referrals around Europe, since the attitudes are quite different among different areas and different regions

The document can be freely downloaded from the ESP website(http://www.esp-pathology.org/pdf/GYN%20WG%20Recommendations%20PoPr.pdf).

We warmly invite you to diffuse the guidelines in your practice and in your country.

For this year, we are focussing on a questionnaire relative to the sampling and the reporting of cervical, vaginal, and vulvar pathology : the questionnaire will be sent soon to the Group Members. We would like to prepare a survey on the different ways of sampling and working in this area and we hope to be able to present and discuss the results at the next Lisbon ESP Congress.

Our Chair Harry Hollema has worked hard to provide the Prague Congress with excellent sessions on Gynaecological Pathology. All were highly scientific and very well attended and we are also thankful to our members who have provided unusual cases discussed in a specific session. He has also finalised the program of the next Lisbon Congress: the leitmotiv this year will be the patology of cervix. Again some of you have already submitted excellent difficult cases for discussion and I forecast a very lively session.

Looking forward to see you many in Lisbon in September

Best personal regards,

Maria Rosaria Raspollini Secretary/Elected Chair
Gynaecological Pathology Working Group

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Analecta Medica
Dr. Loukas Kaklamanis

1)

Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis

Mackenzie R Wehner, Melissa L Shive, Mary-Margaret Chren,Jiali Han, Abrar A Qureshi, Eleni Linos.

BMJ 2012; 345: e5909 doi: 10.1136/bmj.e5909.

Abstract

Objective To synthesise the literature on indoor tanning and non-melanoma skin cancer.

Design Systematic review and meta-analysis.

Data sources PubMed (1966 to present), Embase (1974 to present), and Web of Science (1898 to present).

Study selection All articles that reported an original effect statistic for indoor tanning and non-melanoma skin cancer were included. Articles that presented no data, such as review articles and editorials, were excluded, as were articles in languages other than English.

Data extraction Two investigators independen-tly extracted data. Random effects meta-analysis was used to summarise the relative risk of ever use versus never use of indoor tanning. Dose-response effects and exposure to indoor tanning during early life were also examined. The population attributable risk fraction for the United States population was calculated.

Results 12 studies with 9328 cases of non-melanoma skin cancer were included. Among people who reported ever using indoor tanning compared with those who never used indoor tanning, the summary relative risk for squamous cell carcinoma was 1.67 (95% confidence interval 1.29 to 2.17) and that for basal cell carcinoma was 1.29 (1.08 to 1.53). No significant heterogeneity existed between studies. The population attributable risk fraction for the United States was estimated to be 8.2% for squamous cell carcinoma and 3.7% for basal cell carcinoma. This corresponds to more than 170□000 cases of non-melanoma skin cancer each year attributable to indoor tanning. On the basis of data from three studies, use of indoor tanning before age 25 was more strongly associated with both squamous cell carcinoma (relative risk 2.02, 0.70 to 5.86) and basal cell carcinoma (1.40, 1.29 to 1.52).

Conclusions Indoor tanning is associated with a significantly increased risk of both basal and squamous cell skin cancer. The risk is higher with use in early life (<25 years). This modifiable risk factor may account for hundreds of thousands of cases of non-melanoma skin cancer each year in the United States alone and many more worldwide. These findings contribute to the growing body of evidence on the harms of indoor tanning and support public health campaigns and regulation to reduce exposure to this carcinogen.

2)

Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis

Mathieu Boniol,Philippe Autier, Peter Boyle, Sara Gandini.

BMJ 2012;345: **e4757.** doi: 10.1136/bmj.e4757.

Abstract

Objective To estimate the burden of melanoma resulting from sunbed use in Western Europe.

Design Systematic review and meta-analysis.

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Data sources PubMed, ISI Web of Science (Science Citation Index Expanded), Embase, Pascal, Cochrane Library, LILACS, and MedCarib, along with published surveys reporting prevalence of sunbed use at national level in Europe.

Study selection Observational studies reporting a measure of risk for skin cancer (cutaneous melanoma, squamous cell carcinoma, basal cell carcinoma) associated with ever use of sunbeds.

Results Based on 27 studies ever use of sunbeds was associated with a summary relative risk of 1.20 (95% confidence interval 1.08 to 1.34). Publication bias was not evident. Restricting the analysis to cohorts and population based studies, the summary relative risk was 1.25 (1.09 to 1.43). Calculations for dose-response showed a 1.8% (95% confidence interval 0% to 3.8%) increase in risk of melanoma for each additional session of sunbed use per year. Based on 13 informative studies, first use of sunbeds before age 35 years was associated with a summary relative risk of 1.87 (1.41 to 2.48), with no indication of heterogeneity between studies. By using prevalence data from surveys and data from GLOBOCAN 2008, in 2008 in the 15 original member countries of the European Community plus three countries that were members of the European Free Trade Association, an estimated 3438 cases of melanoma could be attributable to sunbed use, most (n=2341) occurring among women.

Conclusions Sunbed use is associated with a significant increase in risk of melanoma. This risk increases with number of sunbed sessions and with initial usage at a young age (<35 years). The cancerous damage associated with sunbed use is substantial and could be avoided by strict regulations.

3)

Atherosclerosis across 4000 years of human history: the Horus study of four ancient populations

Thompson RC, Allam AH, Lombardi GP, Wann LS, Sutherland ML, Sutherland JD, Soliman MA, Frohlich B, Mininberg DT, Monge JM, Vallodolid CM, Cox SL, Abd el-Maksoud G, Badr I, Miyamoto MI, el-Halim Nur el-Din A, Narula J, Finch CE, Thomas GS.

Lancet 2013; 381:1211. doi: 10.1016/S0140-6736(13)60598-X.

Summary

Background

Atherosclerosis is thought to be a disease of modern human beings and related to contemporary lifestyles. However, its prevalence before the modern era is unknown. We aimed to evaluate preindustrial populations for atherosclerosis.

Methods

We obtained whole body CT scans of 137 mummies from four different geographical regions or populations spanning more than 4000 years. Individuals from ancient Egypt, ancient Peru, the Ancestral Puebloans of southwest America, and the Unangan of the Aleutian Islands were imaged. Atherosclerosis was regarded as definite if a calcified plaque was seen in the wall of an artery and probable if calcifications were seen along the expected course of an artery.

Findings

Probable or definite atherosclerosis was noted in 47 (34%) of 137 mummies and in all four geographical populations: 29 (38%) of 76 ancient Egyptians, 13 (25%) of 51 ancient Peruvians, two (40%) of five Ancestral Puebloans, and three (60%) of five Unangan hunter gatherers (p=NS). Atherosclerosis was present in the aorta in 28 (20%) mummies, iliac or femoral arteries in 25 (18%), popliteal or tibial arteries in 25 (18%), carotid arteries in 17 (12%), and coronary arteries in six (4%). Of the five vascular beds examined, atherosclerosis was present in one to two beds in 34 (25%) mummies, in three to four beds in 11 (8%), and in all five vascular beds in two (1%). Age at time of death was positively correlated with atherosclerosis (mean age at death was 43 [SD 10] years for mummies with atherosclerosis *vs* 32 [15] years for those without; p<0·0001) and with the number of arterial beds involved (mean age was 32 [SD 15] years for mummies with no atherosclerosis, 42 [10] years for those with atherosclerosis in one or two beds, and 44 [8] years for those with atherosclerosis in three to five beds; p<0·0001).

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Interpretation

Atherosclerosis was common in four preindustrial populations including preagricultural hunter-gatherers. Although commonly assumed to be a modern disease, the presence of atherosclerosis in premodern human beings raises the possibility of a more basic predisposition to the disease.

4)

Analysis of Circulating Tumor DNA to Monitor Metastatic Breast Cancer

Dawson SJ, Tsui DW, Murtaza M, Biggs H, Rueda OM, Chin SF, Dunning MJ, Gale D, Forshew T, Mahler-Araujo B, Rajan S, Humphray S, Becq J, Halsall D, Wallis M, Bentley D, Caldas C, Rosenfeld N.

N Engl J Med 2013; 368:1199. doi:10.1056/NEJMoa1213261.

BACKGROUND

The management of metastatic breast cancer requires monitoring of the tumor burden to determine the response to treatment, and improved biomarkers are needed. Biomarkers such as cancer antigen 15-3 (CA 15-3) and circulating tumor cells have been widely studied. However, circulating cell-free DNA carrying tumor-specific alterations (circulating tumor DNA) has not been extensively investigated or compared with other circulating biomarkers in breast cancer.

METHODS

We compared the radiographic imaging of tumors with the assay of circulating tumor DNA, CA 15-3, and circulating tumor cells in 30 women with metastatic breast cancer who were receiving systemic therapy. We used targeted or whole-genome sequencing to identify somatic genomic alterations and designed personalized assays to quantify circulating tumor DNA in serially collected plasma specimens. CA 15-3 levels and numbers of circulating tumor cells were measured at identical time points.

METHODS

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RESULTS

Circulating tumor DNA was successfully detected in 29 of the 30 women (97%) in whom somatic genomic alterations were identified; CA 15-3 and circulating tumor cells were detected in 21 of 27 women (78%) and 26 of 30 women (87%), respectively. Circulating tumor DNA levels showed a greater dynamic range, and greater correlation with changes in tumor burden, than did CA 15-3 or circulating tumor cells. Among the measures tested, circulating tumor DNA provided the earliest measure of treatment response in 10 of 19 women (53%).

CONCLUSIONS

This proof-of-concept analysis showed that circulating tumor DNA is an informative, inherently specific, and highly sensitive biomarker of metastatic breast cancer. (Funded by Cancer Research UK and others.)

5)

Focal segmental glomerulosclerosis is induced by microRNA-193a and its downregulation of WT1

Gebeshuber CA, Kornauth C, Dong L, Sierig R, Seibler J, Reiss M, Tauber S, Bilban M, Wang S, Kain R, Böhmig GA, Moeller MJ, Gröne HJ, Englert C, Martinez J, Kerjaschki D.

Natutre Medicine 2013; 19:481. doi: 10.1038/nm.3142.

ABSTRACT

Focal segmental glomerulosclerosis (FSGS) is a frequent and severe glomerular disease characterized by destabilization of podocyte foot processes. We report that transgenic expression of the microRNA miR-193a in mice rapidly induces FSGS with extensive podocyte foot process effacement. Mechanistically, miR-193a inhibits the expression of the Wilms' tumor protein (WT1), a transcription factor and master regulator of podocyte differentiation and homeostasis.

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Decreased expression levels of WT1 lead to downregulation of its target genes *PODXL* (podocalyxin) and *NPHS1* (nephrin), as well as several other genes crucial for the architecture of podocytes, initiating a catastrophic collapse of the entire podocyte-stabilizing system. We found upregulation of miR-193a in isolated glomeruli from individuals with FSGS compared to normal kidneys or individuals with other glomerular diseases. Thus, upregulation of miR-193a provides a new pathogenic mechanism for FSGS and is a potential therapeutic target.

6)

Characterisation of retinoblastomas without RB1 mutations: genomic, gene expression, and clinical studies

Rushlow DE, Mol BM, Kennett JY, Yee S, Pajovic S, Thériault BL, Prigoda-Lee NL, Spencer C, Dimaras H, Corson TW, Pang R, Massey C, Godbout R, Jiang Z, Zacksenhaus E, Paton K, Moll AC, Houdayer C, Raizis A, Halliday W, Lam WL, Boutros PC, Lohmann D, Dorsman JC, Gallie BL.

Lancet Oncology 2013; 14:327. doi: 10.1016/S1470-2045(13)70045-7.

SUMMARY

BACKGROUND

Retinoblastoma is the childhood retinal cancer that defined tumour-suppressor genes. Previous work shows that mutation of both alleles of the *RB1* retinoblastoma suppressor gene initiates disease. We aimed to characterise non-familial retinoblastoma tumours with no detectable *RB1* mutations.

METHODS

Of 1068 unilateral non-familial retinoblastoma tumours, we compared those with no evidence of *RB1* mutations (*RB1*+/+) with tumours carrying a mutation in both alleles (*RB1*−/−). We analysed genomic copy number, *RB1* gene expression and protein function, retinal gene expression, histological features, and

FINDINGS

No *RB1* mutations (*RB1*+/+) were reported in 29 (2·7%) of 1068 unilateral retinoblastoma tumours. 15 of the 29 *RB1*+/+ tumours had high-level *MYCN* oncogene amplification (28—121 copies; *RB1*+/+*MYCNA*), whereas none of 93 *RB1*−/− primary tumours tested showed *MYCN* amplification (p<0·0001). *RB1*+/+*MYCNA* tumours expressed functional RB1 protein, had fewer overall genomic copy-number changes in genes characteristic of retinoblastoma than did *RB1*−/− tumours, and showed distinct aggressive histological features. *MYCN* amplification was the sole copy-number change in one *RB1*+/+*MYCNA* retinoblastoma. One additional *MYCNA* tumour was discovered after the initial frequencies were determined, and this is included in further analyses. Median age at diagnosis of the 17 children with *RB1*+/+*MYCNA* tumours was 4·5 months (IQR 3·5—10), compared with 24 months (15—37) for 79 children with non-familial unilateral *RB1*−/− retinoblastoma.

INTERPRETATION

Amplification of the *MYCN* oncogene might initiate retinoblastoma in the presence of non-mutated *RB1* genes. These unilateral *RB1*+/+*MYCNA* retinoblastomas are characterised by distinct histological features, only a few of the genomic copy-number changes that are characteristic of retinoblastoma, and very early age of diagnosis.

7)

Early detection of cancer in the general population: a blinded case–control study of p53 autoantibodies in colorectal cancer

Pedersen JW, Gentry-Maharaj A, Fourkala EO, Dawnay A, Burnell M, Zaikin A, Pedersen AE, Jacobs I, Menon U, Wandall HH.

British Journal of Cancer 2013; 108:107. doi: 10.1038/bjc.2012.517.

Abstract

BACKGROUND

Recent reports from cancer screening trials in high-risk populations suggest that autoantibodies can be detected before clinical diagnosis. However, there is minimal data on the role of autoantibody signatures in cancer screening in the general population.

METHODS

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Informative p53 peptides were identified in sera from patients with colorectal cancer using an autoantibody microarray with 15-mer overlapping peptides covering the complete p53 sequence. The selected peptides were evaluated in a blinded case–control study using stored serum from the multimodal arm of the United Kingdom Collaborative Trial of Ovarian Cancer Screening where women gave annual blood samples. Cases were postmenopausal women who developed colorectal cancer following recruitment, with 2 or more serum samples preceding diagnosis. Controls were age-matched women with no history of cancer.

RESULTS

The 50 640 women randomised to the multimodal group were followed up for a median of 6.8 (inter-quartile range 5.9–8.4) years. Colorectal cancer notification was received in 101 women with serial samples of whom 97 (297 samples) had given consent for secondary studies. They were matched 1:1 with 97 controls (296 serial samples). The four most informative peptides identified 25.8% of colorectal cancer patients with a specificity of 95%. The median lead time was 1.4 (range 0.12–3.8) years before clinical diagnosis.

CONCLUSION

Our findings suggest that in the general population, autoantibody signatures are detectable during preclinical disease and may be of value in cancer screening. In colorectal cancer screening in particular, where the current need is to improve compliance, it suggests that p53 autoantibodies may contribute towards risk stratification.

Dr. Loukas Kaklamanis

What's new?

Does Red Meat Consumption Induce Atherosclerosis? Impressive New Data Come to Light

Dr. Loukas Kaklamanis

New impressive data, published online in 7th of April 2013 at ***Nature Medicine***, http://dx.doi.org/10.1038/nm.3145(2013), by *RA. Koeth, Z.Wang et al* under the title "Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis", implicate bacteria normally found in the gut, to convert a common compound found in red meat, into a molecule which fascilitates and accelerates atherosclerosis in arterial walls.

In their article Researchers from Cleveland Clinic, Ohio, Perelman School of Medicine, University of Pennsylvania and Wake Forest School of Medicine, in North Carolina, analysed results both from animal studies and human tests. In their study they state:
"Intestinal microbiota metabolism of choline and phosphatidylcholine produces trimethylamine (TMA), which is further metabolized to a proatherogenic species, trimethylamine-*N*-oxide (TMAO). We demonstrate here that metabolism by intestinal microbiota of dietary L-carnitine, a trimethylamine abundant in red meat, also produces TMAO and accelerates atherosclerosis in mice. Omnivorous human subjects produced more TMAO than did vegans or vegetarians following ingestion of L-carnitine through a microbiota-dependent mechanism.

The presence of specific bacterial taxa in human feces was associated with both plasma TMAO concentration and dietary status. Plasma L-carnitine levels in subjects undergoing cardiac evaluation (*n* = 2,595) predicted increased risks for both prevalent cardiovascular disease (CVD) and incident major adverse cardiac events (myocardial infarction, stroke or death), but only among subjects with concurrently high TMAO levels. Chronic dietary L-carnitine supplementation in mice altered cecal microbial composition, markedly enhanced synthesis of TMA and TMAO, and increased atherosclerosis, but this did not occur if intestinal microbiota was concurrently suppressed. In mice with an intact intestinal microbiota, dietary supplementation with TMAO or either carnitine or choline reduced *in vivo* reverse cholesterol transport.

Intestinal microbiota may thus contribute to the well-established link between high levels of red meat consumption and CVD risk."

In news released by Chris Woolston, Nature, earlier on this month, Stanley Hazen, the senior author of the study and Chairman of the Cardiovascular Medicine at the Cleveland Clinic, believes that " bacteria make a whole slew of molecules from food and those molecules can have a huge effect on our metabolic processes" implying that the study could signal a new approach to diet and health.

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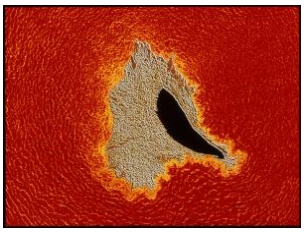

A chemical found in red meat can encourage the growth of fatty deposits (grey) on the walls of arteries (orange) PASIEKA/SCIENCE PHOTO LIBRARY

Photo published by Nature/News by C.Woolston, 7th April 2013

L-carnitine, normally found in red meat, increases the serum levels of trimethylamine-N-oxide (TMAO) which alters the metabolism of cholesterol resulting in increased atherosclerosis. Vegans and vegetarians even when they take L-carnitine, they produce less TMAO than meat eaters. Their faecal studies showed very different types of bacteria in their intestines.

In their animal studies, mice fed with L-carnitine doubled the risk of arterial plaque formation. When the mice were also fed with intestinal-clearing antibiotics, L-carnitine did not inrease the risk of atherosclerosis.

These fascinating results, provided that could be validated in larger perspective studies, might have a major impact in changing human approach to diet.

Dr. Loukas Kaklamanis

1st NordiQC Conference on Standardization in Applied Immunohistochemistry

1st NordiQC Conference on Standardization in Applied immunohistochemistry, June 4th -7th 2013

All information is available on www.nordiqc2013.dk

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MORE QUESTIONS?

Please contact the organizers:
helmut.popper@medunigraz.at; Phone 0043 (0) 316 380 4405
edith.kleinferchner@medunigraz.at; Phone 0043 (0) 316 380 4407

GETTING TO GRAZ BY PLANE

For scheduled flights to Graz see http://www.flughafen-graz.at

MORE INFORMATION ABOUT GRAZ

http://www.graztourismus.at

The course is approved by EScoP
the European School of Pathology
European Society of Pathology

Zeiss Austria will provide the microscopes for the course

ZEISS

Medical University of Graz

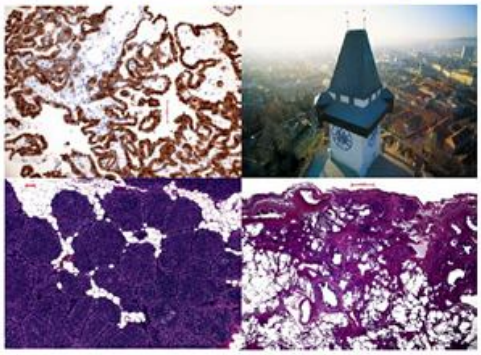
POSTGRADUATE COURSE

LUNG & PLEURAL DISEASES

WITH VIRTUAL MICROSCOPY

Graz, Austria

Part I (Tumour Pathology) June, 20 – 22, 2013
Part II (Non-tumour Pathology) June, 24 – 26, 2013



Course Director
Helmut H. Popper, MD
Institute of Pathology – Medical University of Graz, Austria

Course Faculty
Bruno Murer, MD
Department of Anatomic Pathology – General Hospital Mestre, Italy

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

ADULT CARDIOVASCULAR PATHOLOGY

Thursday 16 – Friday 17 May 2013

NHLI Education Centre
National Heart and Lung Institute
Imperial College London, Dovehouse Street, London SW3 6LY

Course Organiser: Dr Mary Sheppard
www.imperial.ac.uk/medicine/people/mary.sheppard/

This course approaches the practical problems that face the diagnostic pathologist when dealing with cardiovascular pathology, which is the most common cause of death in the western world today. The approach to a cardiac autopsy, cardiac anatomy and cardiac dissection will be emphasised. Topics covered include: sudden cardiac death, valvular heart disease, cardiomyopathies, inherited cardiac disease, myocarditis, and post-operative deaths. A large collection of cardiac specimens and a cardiac pathology museum are also included for study during the two day course.

Course fees: £325 Full Rate | £175 Daily Rate |
£225 Special Rate for SpRs | £120 Special Daily Rate for SpRs

CPD Credits Sought

Course Programme, Faculty List, and Online Registration at www.imperial.ac.uk/nhli/acp/

BOERHAAVE NASCHOLING

Pathology and underlying genetics of inheritable human cancer and developmental defects

25 and 26 April 2013
Leiden

www.boerhaavenascholing.nl

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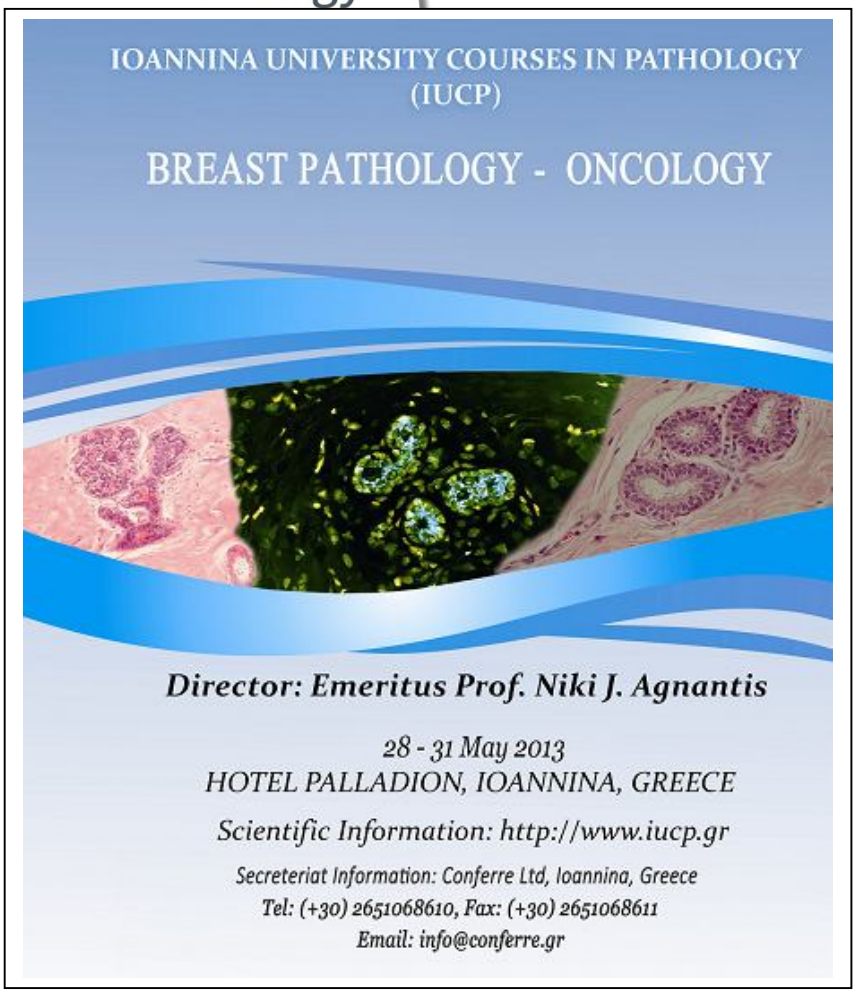

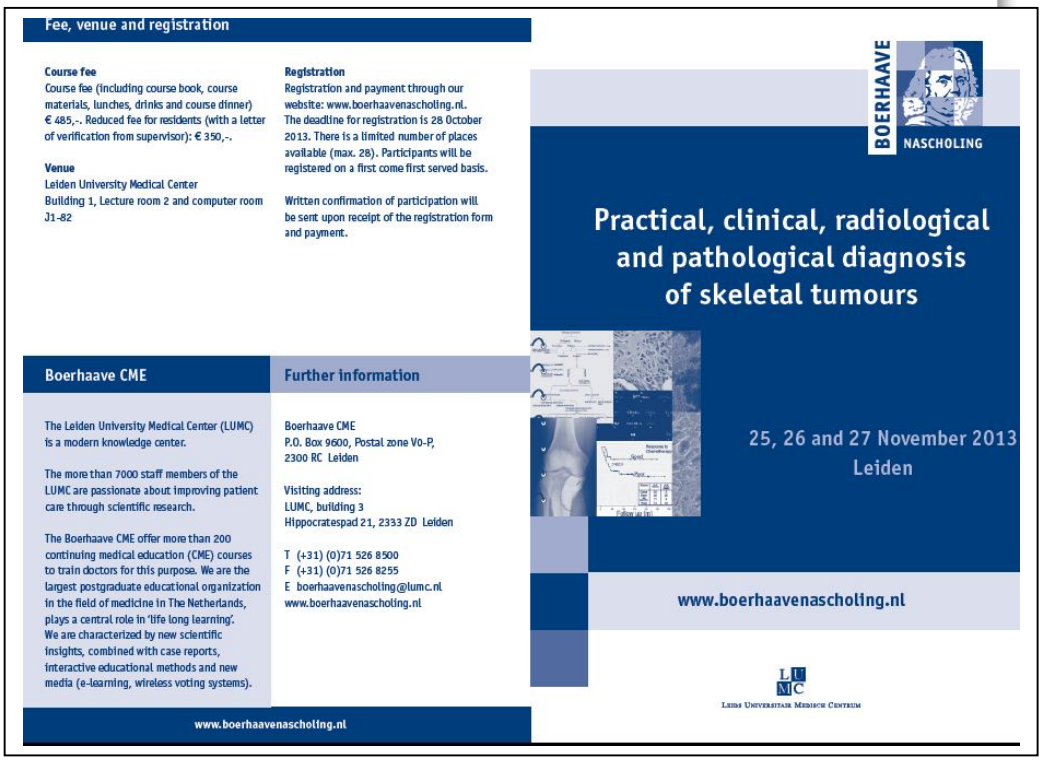

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Basel Seminars in Pathology

Postgraduate Course
Kidney and Urinary Tract
Basel, June 7-8, 2013

Guest Speakers:

Mahul B. Amin
Cedars-Sinai Medical Center, Los Angeles, USA

Peter A. Humphrey
Washington University School of Medicine, St. Louis, USA

Holger Moch
University Hospital Zürich, Switzerland

Ian S. Roberts
John Radcliffe Hospital, Oxford, United Kingdom

Thomas C. Gasser
Urologische Universitätsklinik Basel - Liestal, Switzerland

For additional information contact Helmut Hopfer (Helmut.Hopfer@usb.ch) or see our website (http://pathologie.unispital-basel.ch, "Aktuelles"

Kidney and Urinary Tract - Postgraduate Course
One and a half day course with lectures and interactive sessions for surgical pathologists. Up-to-date information on neoplastic and non-neoplastic diseases of the kidney and the urinary tract.

When:
Starts: Friday, June 7, 2013, 9:00 h.
Ends: Saturday, June 8, 2013, 14:00 h.

Where:
Pathology, University Hospital Basel, Schönbeinstrasse 40, CH-4031 Basel, Switzerland

Course costs and registration:
CHF 100.- (including seminars, workshops, lunch, buffet, and refreshments). Please see our website: http://pathologie.unispital-basel.ch, "Aktuelles/Basel Seminars in Pathology"

Organization
Lukas Bubendorf, Basel, Switzerland
Helmut Hopfer, Basel, Switzerland

Speakers
Ian S. Roberts, Oxford, United Kingdom
Holger Moch, Zürich, Switzerland
Mahul B. Amin, Los Angeles, U.S.A.
Peter A. Humphrey, St. Louis, U.S.A.
Thomas C. Gasser, Basel/Liestal, Switzerland

Basel Seminars in Pathology

Renal Transplant Pathology
Hands-on Course, June 3 - 6, 2013

Kidney and Urinary Tract
Postgraduate Course, June 7 - 8, 2013