## Newsletter

## March 2019

## History of Pathology Society Officers

President: Susan Lester
President-Elect: Henry Tazelaar
Past President: Gabriella Nesi
Secretary-Treasurer: Santo V. Nicosia

Trustees:
Daniel Kurtycz (2018-2021)
Fabio Zampieri (2018-2021)
Stephen A. Geller (2017-2020)

History of Pathology Society Meeting
Gaylord Resort \& Convention Center, National Harbor, MD, USA
Sunday, March 17, 2019, 3:30-5:30 p.m.
United States and Canadian Academy of Pathology Meeting

## Molecular Insights into Our Historical Past: Medical Museum Collections as Irreplaceable Biorepositories

Moderator, Susan Lester, MD, PhD, Brigham and Women's Hospital, Boston, MA

## Course Description

Medical museum specimens provide a window into our historical past as revealed by information on human pathogens, inherited disease, and tumor biology. Unfortunately, the few surviving collections may be in peril due to challenges in maintaining specimens and a lack of appreciation of their value. This session will review the state of historical biorepositories in the United States, Canada, and Europe, discuss important studies on historical specimens, and suggest steps that can be taken to preserve these irreplaceable resources.

| 3:30 | Overview of Historical Collections in the United States and Canada <br> Julie Lemmon, MD, Sumner Regional Medical Center, Gallatin, TN |
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| 3:45 | The 1918 Influenza Virus: How Understanding a Scourge of the Past Informs <br> Our Future <br> Jeffery Taubenberger, MD, PhD, National Institute of Health, DC |
| $4: 15$ | European Historical Collections and their Role in Biomedical Research <br> Gabriella Nesi, MD, PhD, University of Florence, Italy |
| $4: 45$ | The Future of Our Past: A Call to Action to Preserve Our Medical Heritage <br> Susan Lester, MD, PhD, Brigham and Women's Hospital, Boston, MA <br> Julie Lemmon, MD, Sumner Regional Medical Center, Gallatin, TN |
| $5: 00$ | Business Meeting |

Molecular Insights into Our Historical Past: Medical Museums as Irreplaceable Biorepositories

History of Pathology Society - 2019
Moderated by President Susan C. Lester, MD, PhD

## XUSCAP



## Schedule

- Overview of Historical Medical Museum Collections in the United States and Canada
- Julie Lemmon, MD
- The 1918 Influenza Virus: How Understanding a Scourge of the Past Informs Our Future
- Jeffery Taubenberger, MD PhD- National Institute of Health
- European Historical Collections and their Role in Biomedical Research
- Gabriella Nesi, MD PhD- University of Florence
- The Future of Our Past: A Call to Action to Preserve Our Medical Heritage
- Susan Lester, MD PhD- Harvard Medical School/Brigham and Women's Hospital


## Overview of Historical Medical Museum Collections in the United States and Canada

Julie Lemmon, MD

## The Rise of Medical Museums

- Historical necessity
- Scarcity of teaching materials
- Flexner Report- 1910


## The Fate of Medical Museums?

- Shifting focus of medical education
- Ability to reproduce and share images
- Expense of maintenance and valuable real estate


## Medical Museums Today- Pilot Study

- Identify existing US and Canadian biorepositories
- Today's uses
- Future: increase accessibility, provide collaboration


## Medical Museums Today- Pilot Study

- Historic museum specimens that retain biomolecules (pre-1970)
- Primarily wet specimens (tissue in fixative)
- Osteological specimens
- Slides
- Blocks


## Medical Museums Today- Pilot Study

- 70 medical museums documented to exist prior to 1970 s
- Noted in Flexner Report, Billings
- Lester, Lemmon, Hall, and Wright investigated collections
- 13 still exist, at least partially catalogued


## Medical Museums Today- Pilot Study

$-80 \%$ discarded or lost to history

## Medical Museums Today- Pilot Study

- Traditional uses
- Teaching
- Research
- Community engagement
- Emerging use: historical biorepository


## Medical Museums Today- Pilot Study

- 12 of 13 available for research
- 6 of 13 currently involved in modern biomedical research


Harvey Cushing Treated the First Known Patient With Carney Complex

Cynthia J. Tsay, ${ }^{1}$ Constantine A. Stratakis, ${ }^{2}$ Fabio Rueda Faucz, ${ }^{2}$ Edra London, ${ }^{2}$
Chaido Stathopoulou, ${ }^{2}$ Michael Allgauer, ${ }^{3}$ Martha Quezado, ${ }^{3}$ Terry Dagradi, ${ }^{4}$ Dennis D. Spencer, ${ }^{5}$ and Maya Lodish ${ }^{2}$
Tsay, CJ, et al, Journal of the Endocrine Society, 1:1312, 2017


Earliest documentation of a patient with Carney Complex by DNA sequencing.

Dr. Harvey Cushing Brain Collection - Yale University


Th NEW ENGLAND JOURNAL Of MEDICINE

BRIEF REPORT

Second-Pandemic Strain of Vibrio cholerae from the Philadelphia Cholera Outbreak of 1849

Alison M. Devault, M.A., G. Brian Golding, Ph.D., Nicholas Waglechner, M.Sc., Jacob M. Enk, M.Sc, Melanie Kuch, M.Sc, Joseph H. Tien, Ph.D, Mang Shi, M. Phil David N. Fisman, M.D., M.P.H., Anna N. Dhody, M.F. S., Stephen Forrest, M.Sc. Kirsten 1. Bos, Ph.D., David J.D. Earn, Ph.D. Edward C. Holmes, Ph.D and Hendrik N. Poinar, Ph.D.


Devault AM, et al, New England Journal of Medicine 370:334-340, 2014.
Vibrio cholera DNA recovered from an intestinal specimen of a victim of the 1849 cholera epidemic demonstrated changes that could be associated with greater pathogenic capacity.

Mutter Museum

UNLOCKING<br>TYOURINGENUITY

The 1918 Influenza Virus: How Understanding a Scourge of the Past Informs Our Future


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Jeffery K. Taubenberger, M.D., Ph.D


## 1918 Influenza Pandemic



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Alergy and
Infectious Dosasen

## 1918 'Spanish’ Influenza Mortality

- Total global deaths in the 9 months of the pandemic in 1918-1919 estimated to be 50-100 million ${ }^{\ddagger, *}$
$\square$ U.S. Deaths = 675,000
$\square$ Flu deaths in Philadelphia in October $1918=10,959$. Total flu deaths $=15,785$
$\square$ U.S. Military deaths to flu $=43,000$ (out of $\sim 100,000$ U.S. Troop casualties in WWI)
- Deaths in Virginia = 17,604; in Richmond = 1240 (~1\% of population)


## US Soldiers with 1918 Influenza, Ft. Riley, KS



## 1918 Influenza Pandemic Waves



## Death Registry, Oregon 1918-19





## Unique 1918 Age-Specific Mortality



## Influenza A virus

\% Family: Orthomyxoviridae
-Negative sense, segmented, single-stranded RNA genome

- 8 segments, at least $12-13$ ORF's


"Shift and Drift"


Influenza A Virus Host Range Quite Diverse



## Influenza Pandemics in History

- ~14 pandemics in last 500 years
- Average interpandemic period $\sim 36$ years



## Hunting for the 1918 Influenza Virus

- Concept of viruses as infectious agents still new in 1918
$\square$ No isolates of virus made during pandemic
Influenza A viruses first isolated from pigs in 1930 and from humans in 1933


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## 1918 Influenza Autopsy Cases




## 1918 Flu in Teller Mission, Alaska

- Teller Mission (now Brevig Mission) was an isolated Inuit village on the Seward Peninsula of Alaska
$\square$ Pandemic hit in November, carried by mail courier (traveling by sled dog)
$\square$ Local outbreak last 5 days
$\square 72$ people killed ( $85 \%$ adult population), leaving dozens of orphans
$\square$ Johan Hultin performed an exhumation in 1951



## 'Resurrecting’ the 1918 Influenza Virus



## 1918 Lung Pathology

Primary Viral Pneumonia: DAD with edema, alveolitis, thrombi


## 1918 Lung Pathology

Secondary Bacterial Pneumonia and Repair


Taubenberger \& Morens 2008 Ann Rev Path 3:499


## 1918 H1N1 Autopsy Study



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- Since 1918 all pandemic and seasonal influenza viruses descended from the 1918 virus
- All influenza mortality in last 100 years ultimately due to one viral introduction


## - Concept of

 'pandemic era'
## Influenza Pathogenicity



## Mapping Virulence of the 1918 Influenza Virus -1918-Avian Single Gene Reassortants

- 1918 HA is the main virulence factor in pathogenicity in mice, ferrets, NHP - 1918 virus has a very avian-like genome
- Avian H1 HAs did not attenuate 1918 virus, and share virulence with 1918
- 1918 virus virulence therefore likely not pandemic virus-specific but inherited from a low path avian H 1 ancestor
$\square$ LPAI gene


What about other low path avian influenza (LPAI) HA subtypes?

## What about other LP Avian HA Subtypes?



B


## LP Avian Virus Mouse Pathogenicity




Pathogenic viruses:

- H1, H6, H7, H10, H15
- Lung titers did not correlate with pathogenicity

ai, et al. 2014 MBio. 5:e02116-14


China reports first human case of H10N8 avian flu

A 73 -year-old woman in Jiangxi province in China has died from an HoN88 avian flu infection, Hong Kong's Centre for Health Protection (CHP) said today, the first report of that strain infecting humans.

The woman, whose immune system was
compromiead had an muliarlvina illnose and hand visited ali statement 30, was di
died Dec $t$
died Dec

## Taiwan reports first human H6N1 infection

Fiod Under: Avien lefluenza (Bind Fily)
Ita Sotriming I Stur Witoo | CIDPNP Noms | Jun 21, 2013
Health authorities in Taiwan today announced the
first known human infection with H6N1 avian
influenza, in a 20 -year-old womr
pneumonia in May and has sino
H7N9 hospitalizes 6 more in China

officials were on heightened aler Lso Sccvimig | Sart What | CDPIP Ness | Jan 17, 2014
The woman's novel flu infection
attention of Taiwanese health of $\mathrm{Six} \mathrm{H}_{7} \mathrm{~N} 9$ influenza infections were reported in two after the region had identified it, Chinese provinces and the city of Shanghai today, man who had recently traveled t keeping the volume of new cases within striking area for work. distance of peak activity the country saw during the outbreak's first wave last spring.

China's National Health and Family Planning Commission today addressed the quickly rising number of $\mathrm{H}_{7} \mathrm{~N} 9$ cases, especially since the first of the year, according a report today from Xinhua, the state news agency. It said 28 cases have been reported so
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Upregulated Inflammatory Responses
During 1918 Infection


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Kash, et al. 2006 Nature 443.578

## Treatment with a Catalytic ROS Scavenger Decreases Lung Damage and Increases Survival



EUK-207: organometallic SOD/catalase mimetic

1918 Pandemic Influenza Virus


## Influenza Pathogenicity



## Viral \& Bacterial Copathogenesis

pH1N1+SP infection associated with loss of basal cells and absence of re-proliferation and repair of airway epithelial cells


Repair/proliferation genes



Viral damage to and loss of airway epithelial cells may expose basal epithelial cells to bacteria leading to the death of these progenitor cells, limiting reproliferation


## 1918 Pneumonia Case with Prominent Erythrocyte Sickling



DNA sequence of the hemoglobin beta gene from the 1918 FFPE lung tissue showed Glu6Val hemoglobin S mutation, 4 years before term "sickle cell anemia" described

## Outstanding 1918 Questions to be Addressed by Archaevirology

Where and when did the 1918 pandemic virus emerge?

- Identification of pre-1918 human influenza pnenumonia autopsy tissues
$\square$ What subtype(s) of influenza circulated before 1918 ?
$\square$ What was the nature of the 1889 pandemic virus?
- Identification of spring-summer wave 1918 cases

Studying early post-pandemic evolution of H1N1 viruses

- Identification of post-1918 human influenza pnenumonia autopsy tissues

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## Flattening of the "W"



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## Next Generation Sequencing of 1918 cDNA



1918 sample library sequenced:

- Complete viral genome at 3000 x coverage, including UTRs
- Host gene and bacterial genes well represented in library
- High bacterial representation of Streptococcaceae (Postmortem lung culture pos. for Strep pneumoniae) \& Pasteurellaceae (H. influenzae)
- 1918 sample significantly enriched for genes related to host defense and cell death responses as compared to a 2009 pandemic autopsy sample


## Positive Enrichment Strategies for Influenza Archaevirology



## Tetravalent Vaccine Provides Broad Protection



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## Acknowledgements and Funding

Viral Pathogenesis and Evolution Section, Laboratory of Infectious Diseases, NIH/NIAID




The creation as well as the revamping of a Museum should be based on the use of multimedia and interactive systems. These should include the possibility to offer to scholars collections of pictures of rare and peculiar cases together with historicaldocumentary information


Museums should be responsible for collecting and safeguarding anatomical specimens of particular interest from a historical and epidemiological point of view

Myocardial Hypertrophy
Pathology Museum of the University of Florence

## Breast Cancer

Pathology Museum of the University of Florence

The results will be used to improve our knowledge of history, location, institutional status, audiences and policies of Pathology Museums across Europe

Preservation of anatomical specimens and facilities is neither easy nor uncostly, and calls for patronage. In order for it to develop, a European Pathology Museum Network should aim to promote the study, access and divulgation of antique collections


## PRELIMINARYRESULTS



| AUSTRALIA |
| :---: |
| AUSTRIA |
| AZERBAIJAN |
| CZECH REPUBLIC |
| GERMANY |
| HUNGARY |
| IRAQI KURDISTAN |
| ITALY |
| REPUBLIC OF MOLDOVA |
| THE NETHERLANDS |
| POLAND |
| PORTUGAL |
| ROMANIA |
| SPAIN |
| TURKEY |
| UKRAINE |
| UNITED KINGDOM |




On 15 June 1888, the German Emperor, Kaiser Friedrich III, died of laryngeal cancer. Three biopsies of his laryngeal lesion had been taken by the British laryngologist, Morel Mackenzie, in 1887 and diagnosed by Rudolf Virchow as "pachydermia verrucosa laryngis", confirming Mackenzie's assessment that the Kaiser's disease was benign. A fourth specimen coughed up by the patient was considered by Virchow to be nondiagnostic. A further specimen expectorated by the patient 3 months before his death was diagnosed as carcinoma by Wilhelm Waldeyer.
The autopsy revealed squamous carcinoma in the larynx with a cervical lymph node metastasis. The discrepancies between the initial diagnoses and the final outcome of the Kaiser's disease gave rise to a never-ending medical controversy. Our investigations on this historical case were limited to the official German documents and publications and their English translations and to subsequent literature sources of the time, after having received confirmation that the histological slides and Virchow's original reports had been lost. Based on current surgical pathology knowledge, we propose that the tumour that challenged the diagnostic skills of the founder of pathology was hybrid verrucous carcinoma (HVC), an extremely rare, metastasizing variant of verrucous carcinoma (VC) composed of pure VC mixed with clusters of conventional squamous cell carcinoma. As we see it now, Virchow was therefore not totally wrong. Our retrospective evaluation suggests that Virchow's detailed description of the Kaiser's cancer preceded the paper that contributed to the full understanding of HVC of the larynx by 110 years

The Kaiser's cancer revisited: was Virchow totally wrong?

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Ahtomio Carden. Nias Ridar - Ilucia Ales -
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Alfons Nadal - Nina Gale - Cianter Klippel


## KRAS mutations in historical tumour specimens of the Viennese Museum of pathological anatomy

Sedivy R, Kalipciyan M, Patzak B, Mader RM


RESEARCH ARTICLE
Molecular and Immunohistochemical Characterization of Historical Long-Term Preserved Fixed Tissues from Different Human Organs

Maja Hühns**, Paula Röpenack, Andreas Erbersdobler








## "Norwegian scabies" in a wax model at the Pathology Museum of the University of Florence

Nesi G, Santi R, Sestini S, De Giorgi V, Taddei GL

The reproduction in wax of anatomic specimens is considered a glorious Italian tradition, particularly in Florence. Indeed, the work of wax masters which was cultivated for ex-votos and statuary models, together with the development of anatomic studies under the guidance of Paolo Mascagni at the end of the eighteenth century, gave origin to several collections of waxes, among which the collection of the Museum of Anatomic Pathology holds undoubted interest. The so-called "leper", a full-scale reproduction by Luigi Calamai of a man affected with Norwegian scabies, a rare skin disease, is considered the symbol of the Museum
"Impetigine scabida complicata da rogna>
Wax Master: Luigi Calamai (1796-1851)

" N. Ordine 1881 Questo preparato eseguito dal Sig. Egisto Tortori sotto la direzione del prof. Augusto Michelacci è il ritratto fedele di una giovane di 25 anni che fu ricoverata nell'ospedale delle malattie cutanee di Firenze nell'anno 1865. Essa era da molti anni ammalata delle scrofulidi che sono rapprsentate nel preparato"

Text from the Original Catalogne of the Museum
"Scrofulide tubervolare verrucose e flemmonosa della facia", A Case of Cutaneous Twbercolosis, IVax Master: Egisto Tortori (1829-1893)


## Art and the teaching of pathological anatomy at the University of Florence since the nineteenth century

Gabriella Nesi - Raffaella Santi - Gian Luigi Taddei

In 1840, the University of Florence was the first university in Italy to confer a Professorship in Pathological Anatomy. The origin of this teaching post is linked to the history of the Pathology Museum founded in 1824 by the Florentine Accademia Medico-Fisica. The Museum houses anatomical specimens and wax works depicting pathological conditions in the nineteenth century. Both the need to instruct medical students in pathology without resorting to corpse dissection and the difficulty of the lengthy preservation of anatomical preparations made it necessary to produce life-sized wax duplicates of diseased parts of the body. Through the history of the Pathology Museum of Florence, we describe how pathology developed and, in particular, how pathologists from a literary circle laid the foundations of modern surgical pathology in Italy. Museum visits for the medical students guided by lecturers are still today a component of the course of Pathological Anatomy


Univentricular Heart in a Newborn Infant
Wax Master: Egisto Tortori (1829-1893)


Ancient DNA (aDNA) Extraction



# The Future of Our Past: A Call to Action to Preserve our Medical Heritage 

Susan C. Lester, MD PhD<br>Julie Lemmon MD

## Save our Specimens

## Outlook for existing collections

- Funding at risk
- Dedicated space difficult to maintain
- Underappreciated and underutilized


## What can we do?

Identify
Support
Brainstorm
Join

# Remaining Collections in United States 

| Collection | Location | Contact |
| :---: | :---: | :---: |
| Warren Anatomical Museum Harvard Medical School | Boston, MA | Dominic Hall MA ALM, Curator |
| The Mütter Museum | Philadelphia, PA | Anna Dhody, Curator |
| The National Museum of Health and Medicine | Silver Spring, MD | Brian Spatola, Curator |
| Mayo Clinic | Rochester, MN | Joseph J. Maleszewski, Director of Tumor Registry Gary L. Keeney, Chairman of Pathology |
| Dr. Harvey Cushing Brain Collection Yale University | New Haven, CT | Melissa Grafe, Curator |
| Old Red Medical Museum - University of Texas | Galveston, TX | Paula Summerly, Research Project Manager |
| Gordon R. Hennigar Pathology Museum Medical University of South Carolina | Charleston, SC | Evelyn T. Bruner, MD |
| University of Maryland | Baltimore, MD | Adam C. Puche |
| Indiana Medical History Museum | Indianapolis, IN | Sarah M. Halter, Executive Director |
| Monroe Moosenick Collection Transylvania University | Lexington, KY | Jamie Day, PhD |

## Remaining Collections in Canada

| Collection | Location | Contact |
| :--- | :--- | :--- |
| Maude Abbott Museum - McGill <br> University | Montreal, QC | Richard Fraser, MD- Director |
| Boyd Pathology Museum - <br> Manitoba Medical College | Winnipeg, MB | Gabor Fischer |
| William Boyd Collection - <br> University of British Columbia | Vancouver, BC | Helen Dyck, Curator |

## IDENTIFY

If you know of other existing collections, let us know -
Julie.Lemmon@gmail.com

## SUPPORT

Advocate - If you are associated with an institution with a historical tissue collection, take opportunities to show your support.

Visit - Many collections are open to the public.
Funding - Consider opportunities to help collections catalog and preserve their holdings.

## BRAINSTORM

Are there other interesting research projects that could be done with historical specimens?

Are there researchers who may not be aware of existing specimens?

Are there are other ways to help preserve these collections?

## JOIN

- Coalition of curators, researchers, pathologists
- North America
- Europe- European Society of Pathology History of Pathology Working Group
- All other locations- similar groups??
- Website to connect and serve as resource
- Collection description, scope, and point of contact
- Resource for research scientists
- Increase visibility
- Send contact information to Julie.Lemmon@gmail.com


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