The Future of Cardiovascular Pathology

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Disclosures

• I am an anatomical pathologist
• I am a cardiovascular pathologist

• I have no financial disclosures but am open to talk

• This talk is my opinion and may cause sleepiness and headache
• It should not be used without consulting your family doctor or health professional
Pathologist = Laboratory Scientist
Our future

• What is happening?

• What is happening in health care?

• How will these changes affect our specialty of pathology?
Pathologist

Pathologists are physicians and scientists who take an *active role in patient care*, utilizing available tools to integrate and interpret diagnostic information to provide an accurate diagnosis of disease.

We work with other members of the health care team to assess the patient condition and prognosis in order to determine optimum therapy alternatives.
Pathologists

- Have a unique knowledge of disease processes
- Are knowledge integrators
- Can get access to and analyze many types of diagnostic data
- Are responsible for the testing that is driving therapy
Cardiovascular pathology history

• A long and great history!

• Society for Cardiovascular Pathology 1985

• European School for Cardiovascular Pathology 1994

• Association for European Cardiovascular Pathology 2004
Where have we been?

Key contributions of CVP

- Recognition of mechanisms of atherosclerosis and its complications
  - Clinical pathological studies
  - Experimental studies
  - Correlation of pathology with imaging

F Schoen Cardiovascular Pathology 2010; 19:198-200
Key contributions of CVP

- Cardiovascular surgical and interventional diagnostic and therapeutic procedures and devices used to manage adult and congenital heart disease
  - Congenital heart repairs and surgeries
  - Adult heart repair and surgery
  - Cardiac transplantation
  - Prostheses
  - Importance of myocardial protection

F Schoen Cardiovascular Pathology 2010;19:198-200
Key contributions of CVP

• Elucidation of molecular mechanisms of disease and especially the impact of genetic abnormalities on many subsets of cardiovascular disease
  – Cardiomyopathies
  – Channelopathies
  – Vascular diseases

F Schoen Cardiovascular Pathology 2010;19:198-200
CVP until 1970s

- Cardiac operations feasible after development of myocardial protection
- Knowledge of congenital heart anatomy
  - Cardiac registries and collections
- Conduction system studies
- Pulmonary vascular disease
- Surgical pathology of the heart and blood vessels
- Valve and vascular prostheses and their complications

G Thiene Kardiovaskuläre Medizin 2010;13(2):41–49
CVP in 1980s

- Interventional cardiology - angioplasty
- Endomyocardial biopsy
- Cardiac transplantation
- Cardiomyopathy classification
- ARVC - arrhythmogenic cardiomyopathy described (ARVD)
- Sudden death studies

G Thiene Kardiovaskuläre Medizin 2010;13(2):41–49
CVP more recent

- Molecular biology
- In situ, PCR, gene sequencing
- Myocarditis
- Apoptosis and cell death
- Channelopathies
- Molecular classification of cardiomyopathy

G Thiene Kardiovaskuläre Medizin 2010;13(2):41–49
What trends will affect our practice?

- Population demographics
- Patient expectations
- New tools - our tools and other’s tools
- Integration of specialities
- Focus upon quality
Trend = Changing demographics

Source: U.S. Census Bureau
Disease and treatment are changing

Aging population

More

• Diseases of degeneration
• Diabetes mellitus, type II
• Heart and renal failure
• Prolonged natural history of diseases

• Cost of health care increasing
Trend = What does the patient/consumer want from us?

- High quality, up to date care
- Minimal inconvenience and easy access
- Fast & accurate information
- Reasonable cost
- Trust & confidence
- Low risk – safe care
What does the patient’s physician want from us?

**Help**
- Fast and accurate results
- Understandable and useful information
- Direction on therapy
Sometimes the health care provider isn’t a physician.

Medical testing board to introduce doctor of nursing certification

Physicians are concerned that the move will lead to scope-of-practice expansions.


Starting this fall, doctor of nursing practice graduates will be able to take a certification test that proponents say will set a national standard for DNPs and add to the profession’s credibility.

The voluntary test, being created by the National Board of Medical Examiners, is based on the medical licensing exam. It will be offered at a time of growing momentum in the DNP movement: About 200 nursing schools are expected to offer the two-year DNP degree by 2015.
Trial and error method of care is less acceptable

- Patient presents with symptoms
- Doctor makes a “most likely” diagnosis, may order tests to confirm, and prescribes a treatment plan (drugs and/or surgery)
- Weight & age may affect drug selection & dosage or other intervention
- Plan works or doesn’t work, +/- side effects?
- Treatment success
- Doctor revises treatment plan
Outcomes - disappointing and costly

<table>
<thead>
<tr>
<th>Category of Disease</th>
<th>% who respond to therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics for pain (Cox-2 inhibitors)</td>
<td>80 %</td>
</tr>
<tr>
<td>Asthma</td>
<td>60 %</td>
</tr>
<tr>
<td>Cardiac Arrhythmias</td>
<td>60 %</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>60 %</td>
</tr>
<tr>
<td>Migraine (acute)</td>
<td>52 %</td>
</tr>
<tr>
<td>Migraine (prophylaxis)</td>
<td>50 %</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>50 %</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>48 %</td>
</tr>
<tr>
<td>HCV</td>
<td>47 %</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>30 %</td>
</tr>
<tr>
<td>Oncology</td>
<td>25 %</td>
</tr>
</tbody>
</table>

Source: Physicians’ Desk Reference; Patient response rates to a major drug in selected categories of therapy
In era of personalized medicine, pathologists have a **direct** impact on patient care...

Cetuximab EGFR Ab

€4,300 for eight weeks

K-ras Testing

Do Not Treat

Treat with Erbitux

Treatment Success

Trend = Shift to personalized medicine

• Provision of care for diseases which can be precisely diagnosed
• Treatment with predictably effective rules based therapies

• *Precise diagnosis must precede predictably effective therapy*
Personalized medicine not new; consider infectious disease therapy

- Microscope and various stains
- Identification of microbes that caused disease
- Tailored antibiotic therapy based on the species of organism
- Molecular subtyping and resistance profile of the involved strain
Cancer is experiencing a similar shift

- 2 types: leukemia & lymphoma
- 1950: Farber develops 1st chemotherapy for leukemia
- 1980: Gleevec, the 1st molecular targeted drug, to treat myeloid leukemia
- 1920-1940: 3 types of leukemia (acute, chronic, pre-leukemia) and 2 types of lymphoma (indolent, aggressive)
- 1990: 38 types of leukemia; 51 types of lymphoma

Source: Mara Aspinall, Genzyme
Personalized medicine

• Diagnosis to **predict risk** of disease
• Monitoring healthy people to detect early signs of disease
• Determining whether a treatment is working

• Producing safer drugs by **predicting potential** for adverse effects earlier
• Targeting groups of people most likely to benefit from a drug, while keeping its use from those who may be harmed by it
Personalized CVP path

• Myocarditis - viral Tx or immunosuppression or immunoenhancement
• Cardiomyopathy – molecular diagnosis ? Tx
• Arrhythmia – channelopathies
• Drug treatment of many CVP diseases
  – Thrombolytics/ anti-platelet
  – Myocardial remodelling / cell death
  – Systemic arterial hypertension
  – Arrhythmias
EMB for myocarditis

**Inflammation (biopsy)**
- > 14 cells/mm²
- PCR for cardiotropic agents positive

**Inflammation (biopsy)**
- > 14 cells/mm²
- PCR for cardiotropic agents negative

**Inflammation (biopsy)**
- < 14 cells/mm²
- PCR for cardiotropic agents positive

**Inflammation (biopsy)**
- < 14 cells/mm²
- PCR for cardiotropic agents negative

- **Viral Myocarditis**
- ? Agent-specific anti-viral therapy

- **Autoimmune Myocarditis**
- Immunosuppressive therapy

- **Viral Cardiomyopathy**
- ? Agent-specific anti-viral therapy

- **No Myocarditis**
- Heart failure and anti-arrhythmic therapy

Maisch et al, *Herz* 2006; 31; 9; 881
Molecular diagnostics is at the core of personalized medicine.

Disease diagnosis early
Before the patient begins to manifest any evidence of illness using traditional tools.
Trend = New technologies & tools

- Molecular Diagnostics
- Pharmacogenomics / Proteomics
- Digital Diagnostics
- Bedside diagnostics
- Nanosensors
Our tools

1595: 1st Compound Microscope

1680s: English Tripod Microscope

Mid-1700s: Cuff-style microscope; 1st to provide ease of use and accurate focusing mechanisms

1899: Ernst Leitz Compound Binocular Microscope

Present: Accessories for DIC, fluorescence, polarized light, phase contrast, and photomicrography
New tools

 Automation and robotics

 Molecular diagnosis and Targeting

 Bioinformatics

 Nanotechnology

 Biomarkers

 Personalized Medicine
Are we/you keeping up?

Early Adopters

Consensus Adopters

Cautious Adopters

Late Adopters

Innovators
Microscopy & imaging

• Virtual slide and computer
• Replace or complement the microscope
• Good image clarity
• Can be quantitative, rather than qualitative
• Easier to store
• More durable than glass
Digital pathology

An opportunity

• rapid and long distance consultations
• knowledge sharing
• virtual discussion
• distance education
Trend = Specialty lines defined by our diagnostic tools are fading

- Distinctions within pathology are already rapidly diminishing - “molecular pathology”
  AP, heme, micro, virology, biochem, genetics
- Traditional lines within and between specialties will continue to gray - hybrids
  Radiology, surgery, pathology
- All specialties will look at new modalities to improve and refine their diagnoses
Autopsy!

- CT used to “enhance” or replace autopsy
- Future - Pathologist and radiologist collaborate/ Pathologist alone
- May create renewed interest
  - Comprehensive documentation
  - Increased understandability
  - Non-infectious, non-invasive procedure
  - Efficient, targeted minimally invasive autopsy
  - Less intrusive for families with religious concerns
Trend = Information overload!

Doctors and patients overloaded

Older doctors are not keeping up to date clinically, study says

UK Junior Doctors Ordering Lab Tests They Can’t Interpret

...time devoted to pathology and clinical lab testing in medical school is often not adequate to teach new physicians to be... competent and confident in ordering the right tests... and respond to the lab test results with the correct, recommended actions
Pathologist = Diagnostic Intelligence expert

- We blend knowledge of pathology, disease related molecular processes, and lab diagnostics
- We can be the integrators of information related to the molecular, biochemical, and cellular processes underlying the patient’s disease, complications and symptoms
Trend = Quality and safety

• Is our speciality full of divergent methods and opinions?
• Do we have standards for our speciality?
• How do we monitor quality?
• Are we reproducible?

• Are we safe?
Breast Cancer Test Errors Cause Faulty Treatment

January 4, 2008, 8:09 am
Posted by Jacob Goldstein

The era of personalized medicine won’t work unless we can also find our way into the era of reliable diagnostic testing. And in the case of breast cancer—one of the diseases with good personalized drugs for certain types of tumors—the diagnostic tests aren’t working very well, the WSJ reports.

As a result, many women who would benefit from drugs such as Genentech's Herceptin or GlaxoSmithKline's Tykerb are going without because faulty tests say their tumors wouldn’t respond to the drugs. At the same time, errant tests also cause other women are to take drugs that aren’t right for their type of tumor.

"If we tried to market pregnancy tests with this rate of inaccuracy, they would be taken off the market," says Allen Gown, chief pathologist of PhenoPath Laboratories in Seattle, told the WSJ. "It means there are a lot of women being treated inappropriately."

A study published last year and led by Genentech researchers reviewed how well labs performed Her-2 tests, which are used to determine whether a woman should take Herceptin. It found that 14% to 16% of those judged positive for Her-2 were actually negative. Of those judged negative, 18% to 23% were in fact positive.

That sort of high error rate could lead to tighter oversight of labs. The Centers for Medicare and Medicaid Services, the federal agency that regulates the testing sites, is examining tougher quality-control requirements. At the moment, labs have to pass outside proficiency checks on 83 types of tests—a list that was devised 15 years ago and doesn’t include the breast-cancer tests.
“[We're] coming to grips with the fact this isn't a dream. It's more like a nightmare and it looks like it's going to get worse. Suddenly it clicked. This is likely going to get a lot worse before it gets better.”

Andrew Padmos
CEO, Royal College of Physicians and Surgeons of Canada
March 2008
“It’s time to try and fix the problem”

Jagdish Butany, MD
President, Canadian Association of Pathologists

Potential solutions the Canadian medical associations have identified

– Creation of large laboratories where all medical tests in a region would be analyzed by specialists rather than general pathologists
– Mandatory requirement for a 2nd pathologist to sign off on tests showing malignancies
– Creation of standardized terminology, interpretation measures and handling procedures to ensure all lab staff across country use the same thresholds to make a diagnosis
– Requirements for all foreign pathologists to receive the same accreditation in Canada

March 16, 2008
We have a bright future in medicine

- Clinical Consultant
- Researcher/Innovator
- Test Provider
- Interpreter
- Clinical Data Integrator
- Lab Director
- Business Developer
- Practice Leader
The new lab

- Information extracted from minute tissue and fluid samples using complex, automated and miniaturized devices will continue to increase
- Computer based algorithms help integrate information
- Enhanced imaging capabilities will allow groups of pathologists to share information on tissue based diagnostics
We must interact with patients and with other clinicians

- Expand beyond the tissue on the slide – use all diagnostic tools are available
- Broaden our sphere of influence
- Market our services
- Expand your value by influencing prognosis and treatment

...be a part of the treatment team
This is our future

- Personalized medicine
- Virtual pathology
- Information management
- Increased professional overlap and collaboration
- Focus upon quality
...a new mindset

- Provide more than just the diagnosis
- New technology & technology integration
- New practice techniques
- Continuous passion for learning
- New management & soft skills
- Collaborate with others
- Assuming a central important role in the treatment team
Pathology is of great antiquity, but is far from being exhausted. The science of the 19th century has touched it with new vitality, and, with the help of the microscope and chemistry, it is now developing and bearing fruit in a manner which has no parallel in any former part of its long history.

- WH Dickinson Pres. address Pathological Soc London 1899  BMJ Feb 2 1889
Pathology is of great antiquity, but is far from being exhausted. The science of the 21st century has touched it with new vitality, and, with the help of the microscope, imaging and molecular medicine, it is now developing and bearing fruit in a manner which has no parallel in any former part of its long history.
Two things are bad for the heart:
  Running up stairs, and
  Running down people.

Bernard Baruch