LABORATORY MEDICINE: PAST, PRESENT AND FUTURE

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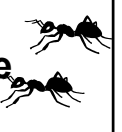
DISCUSSION

- A few reflections on the Past (from centuries ago till mid 70's): physicians mostly did the testing, and the lab directors in the 50's and 60's and 70's designed new tests, and the emphasis was on quality
- The Present: The lab director focuses on dissemination of information and improving efficiency and maintaining high quality
- The Future: The lab Director will focus more on the appropriateness of testing, personalized medicine, and new technologies

THE PAST

First tests known for Diabetes Mellitus

- In 1500 BC Egyptians described excessive urination in the *Papyrus Eber*
- At the same time Hindu doctors noted that bugs were attracted to some patients' urine
- In 1675, the British doctor, Thomas Wills, tasted urine and found it sweet
- In 1750, Scotsman William Cullen added the term "mellitus", the Latin for honey sweet
- In 1962, blood glucose testing strips were first introduced



INSTRUMENTATION IN LABORATORY MEDICINE: 1920

A modern 200-300 bed hospital in the USA would be well equipped if it had. .

- **A balance**
- **A microscope**
- **A centrifuge**
- **A Bunsen burner**
- **A Duboscq colorimeter**

CLINICAL CHEMISTRY IN A HOSPITAL LABORATORY 1970

- **Balance**
- **Spectrophotometer**
- **Flame photometer**
- **Van Slyke apparatus**
- **Klett colorimeter**
- **Centrifuge**
- **New automation**

IN 1970

- There were no calculators. Slide rules were used!

- Little automation
- Very little, if any external quality control
- No fax machines
- No laboratory information systems

AUTOMATION IN CLINICAL CHEMISTRY IS INTRODUCED

- 1957: the first automated analyzer, that was based on continuous flow analysis was introduced by Leonard Skeggs, PhD. It was then produced by the Technicon Corporation. It profoundly changed Clinical Chemistry allowing significant increases in the number of samples that could be processed
- Later the Sequential Multiple Analyzer Computer (SMAC) was introduced. It allowed the testing of multiple analytes (as many as 20) to be analyzed simultaneously
- Since then a myriad of automated Clinical Chemistry Analyzers have been on the market

AUTOMATION IN HEMATOLOGY

- The technology of the Beckman Coulter Counter, formerly known as the Coulter Counter, is based on the Coulter Principle, that was a result of the work of Wallace H. Coulter in 1947
- He demonstrated that an electrical charge could be used to determine the size and number of microscopic particles in a solution
- In the late 60's and early 70's this equipment began to replace manually preparing a blood cell stain and counting each cell under a microscope, a process that typically took 20-30 min

AUTOMATION IN MICROBIOLOGY

- 300 years ago Anton van Leeuwenhoek described bacteria as seen through a microscope
- For most of the last century there were standard cultures, and little automation
- In the last 15 years there has been a shift to more automated systems in microbiology. These yield quicker results, reduce errors and lower turn around time.

INTRODUCTION OF THE CLINICAL LABORATORY IMPROVEMENT ACT (CLIA)

- The objective is to ensure high quality laboratory testing
- 1968 CLIA first introduced, but no enforcement
- I988 amendments were made that stated that the United States Federal Regulatory standards apply to all Clinical Laboratories that perform tests on humans in the US

CLIA Cont'd

- The objective of the amendment was to ensure accuracy, reliability and timeliness of test results wherever the test is performed
- CLIA is frequently updated to incorporate new testing modalities such as genetic and molecular testing
- Currently in 2010 work is being done to update proficiency testing (EQA) requirements

THE PRESENT

- Point-of-Care Testing: this is now a very important part of both outpatient and inpatient settings, and is especially appropriate in developing countries
- Molecular diagnostics
- Sophisticated equipment such as Tandem Mass Spectrometry
- Consolidation of testing single platforms
- Consolidation of reference laboratories

THE PRESENT Cont'd

- Short staffing
- Dramatic increase in POCT and home testing
- Non invasive testing
- Use of Molecular Diagnostics (Chips and SNPs), single cell analyses
- Use of robotics
- Working from home: telecommuting

STAFFING PROBLEMS

STAFFING PROBLEMS

Staffing shortage of 13% nationwide in the US! *WHY*?

- **Medical technology schools closing**
- **Laboratory Medicine technologists and technicians mostly women**
- **Women going into different fields, such as law and medicine**
- **Aging staff, average age nationwide is 51 y**

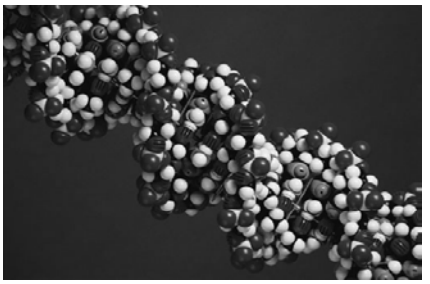
NON INVASIVE TESTING

Glucose

Bilirubin

pH, pO_2, pCO_2

MOLECULAR DIAGNOSTICS



THE IMPORTANCE OF MOLECULAR DIAGNOSTICS

50-70% of medical decisions are thought to be based on laboratory data	**Molecular diagnostics is the fastest growing field within laboratory testing**

Molecular diagnostics gives clinical practitioners a better knowledge understanding of disease, and thereby better approaches to treatment and therapy

MOLECULAR DIAGNOSTICS: BETTER PATIENT CARE

- **Infectious Disease & Resistance Testing**
- **Disease Prevention**
- **Personalized Medicine**

MOLECULAR DIAGNOSTICS: BENEFITS OF THE LAB ON A CHIP

- ➔ Combines all testing needs on one micro array chip
- ➔ Cost-per-test decreases
- ➔ Test flexibility means the lab can meet increasing test demands
- ➔ Technologist time is reduced
- ➔ One workstation means less bench space is occupied

MOLECULAR DIAGNOSTICS: SINGLE CELL ANALYSES FOR PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

Offers an alternative to traditional methods of prenatal diagnosis including chorionic villus sampling and amniocentesis

PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

Allows genetic analysis and selection of embryos to be performed

prior to implantation and pregnancy, and thereby increasing the possibility of a child free of Genetic Disease

REQUIRES THE FOLLOWING STEPS…

- **Production of embryos following an IVF cycle**
- **Growth of the embryos to ~8 cells (day 3)**
- **Biopsy (removal) of embryonic cells (blastomeres) for testing**
- **Capture of DNA, that is amplified (for PCR based tests) or intact nucleus (for FISH based tests)**
- **Interpretation and reporting of results**
- **Transfer of selected embryos into uterus on day 5 post retrieval**

THE FUTURE

- The “Omics”
- Biomarkers
- Ethical issues

THE “-OMICS” REVOLUTION

Proteomics

Pharmacogenomics

Nutrigenomics

Physiogenomics

PROTEOMICS

- It is the large scale study of proteins, particularly their structure and functions
- The proteome is complex. It varies from cell to cell, and is constantly changing through its biochemical interactions with the genome and the environment
- The study of proteomics can lead to a better understanding of the disease process
- To catalog all human proteins is a major challenge for scientists. There is an international collaboration to achieve this goal that is being coordinated by the Human Proteome Organization

THE "OMICS"

- PHARMACOGENICS: Pharmacogenetic tests can predict whether a drug will be effective or cause adverse, or even deadly side effects
- NUTRIGENOMICS: Is the field that examines the response of individuals to compounds in food using genomic and other related technologies Nutrigenomics research looks at how diet interacts with gene expression

PHYSIOGENOMICS

Serum albumin-bound fragments: An archive of Potential Disease Markers

- **A protein fragment has been identified, which is derived from a protein encoded by the BRCA2 cancer associated gene**
- **Protein markers have been identified for Alzheimer's Disease**

1) Lowenthal MS, et al. Clin Chem 2005; 51:1933-45
2) Lopez MF, et al. Clin Chem 2005; 10:1946-54

"OMICS"

- **The ultimate goal would be to have broad- based population testing for health maintenance**
- **However before any testing becomes widespread it will be necessary to do outcomes research**
- **A concern is could information gleaned from SNPS be misused by employers?**

CARDIAC BIOMARKER FOR MYOCARIAL INFARCTION

- **Cardiospecificity is the hallmark of the ideal biomarker, because it definitively improves diagnostic characteristics, from sensitivity for detection to earlier appearance in blood after acute events, and thereby earlier detection of damage**
- **An ideal biomarker must also have clear cut of levels for negativity and positivity**

• Courtesy of M. Panteghini

Cardiac Troponin as the "Ideal Biomarker of Cardiac Necrosis

• **Present only in cardiomyocyte Abundant in cardiac tissue**	➢ **Absolute cardiospecificity and high sensitivity for the damage**
• **Released shortly after necrosis**	➢ **Early diagnosis**
• **Released in direct proportion to the extent of necrosis**	➢ **Estimate of infarct size**
• **Persisting in circulation for days following necrosis**	➢ **Late diagnosis**

[mod. from Panteghini M, Biochim Clin 2007;31:9]

NEW BIOMARKERS BEING RELEASED

- In 2010 a new biomarker has been reported as being a reliable marker for diagnosing mild traumatic brain damage
- It is blood test that identifies unique proteins that spill into the blood stream from damaged brain cells
- Not yet FDA approved
- Could be very helpful in assessing returning soldiers from the wars in Iraq and Afghanistan

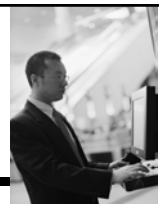
Legal and Ethical Issues

- **The ownership and uses of left-over tissue or any specimens taken from patients**
- **The privacy of laboratory medical records**
- **Problems in publishing, such as plagiarism, or publication of the same paper in different journals**
- **Acceptance of "perks" from companies in return for acquiring an instrument from that same company**

OTHER CHALLENGES FOR THE FUTURE

- More Information technology use
- Implement metrologically correct measurement systems and thereby obtain better traceability
- Use of Nanotechnology
- Reduction of laboratory errors and unnecessary tests
- The changing population demographics in the US and other countries: Ethnic, cultural and racial diversity will change the incidences of major illnesses
- International competition in healthcare

INFORMATION TECHNOLOGY (IT)



- IT needs to be the backbone of healthcare
- It can lead to a better understanding of unnecessary tests by comparing tests ordered with medical usage and outcomes, and thereby decreasing over-utilization
- It allows the development of evidence-based protocols
- Leads to an understanding of the "best" laboratory tests for the diagnosis of disease

INFORMATION TECHNOLOGY

The US is way behind!!

25-30% of hospitals have computerized physician order entry systems for laboratory tests, or electronic medical records

IT IS IMPORTANT TO MOVE FASTER!

METROLOGICALLY CORRECT MEASUREMENT SYSTEMS, AND THEREBY TRACEABILITY

- **This is critical for the future benefit of patients**
- **This has recently been highlighted within IFCC in its development of a reference system for HbA1c, and the definition of correct units**
- **We must reach a use a single established standard for commercial methods for this analyte to better serve diabetic patients**

ADDRESSING QUALITY ISSUES

- Identify areas where errors are likely to occur and then create systems to minimize the possibility of errors
- Address specific errors when they are identified and then create a system to minimize the likelihood of their recurrence

Courtesy of Dr. D. S. Young

NANOTECHNOLOGY: "BIG THINGS FROM A SMALL WORLD"

- It is a relatively new area of science, in which, because of its enormous potential, the US government is supporting research
- It will be used for sensors to detect biological agents
- It will contribute to the diagnosis and therapy of heart, lung and blood disorders by using multiplexed diagnostic sensors to allow the rapid measurement of biomarkers in blood, urine and breath
- There are a huge number of future possibilities from this technology

THE FUTURE

- PERSONALIZED MEDICINE
- PREVENTIVE MEDICINE

NO LONGER "ONE SIZE FITS ALL!

AN EXAMPLE OF PERSONALIZED MEDICINE

- **5-flourouracil (5-FU) is a useful tool in the treatment of breast cancer**
- **However, many patients have severe and even deadly reactions to the drug.**
- **Studies have now identified that there are variations in the gene DPYD that encodes the production of the enzyme dihydropyrimidine dehydrogenase that is responsible for metabolizing 5-FU**
- **There is now a specific test available that can identify patients who will experience severe complications**

Abstracted from AACC Clinical Laboratory Strategies. AACC, Sept 2007

ADVANCING THE CONCEPT OF PERSONALIZED MEDICINE

In May 2007 The National Human Genome Research Institute (part of the National Institutes of Health) in the US announced the following initiative:

- An investigation of the interest level of healthy young adults in receiving genetic testing for seven common conditions
- This study is called the " Multiplex Initiative"

THE MULTIPLEX INITIATIVE

Look at the interest in information regarding 15 different genes that play roles in the following:

- Type II diabetes
- Coronary heart disease
- High blood cholesterol
- Osteoporosis
- Lung cancer
- Colorectal cancer
- Malignant melanoma

THE MULTIPLEX INITIATIVE

- ➔ **This will provide insight into advancing the concept of personalized medicine**
- ➔ **We need to know how such susceptibility testing will be received by individuals**
- ➔ **We need to find out the role this type of testing will play in improving health**
- ➔ **Participants in the study will receive free genetic testing**

PREVENTION: BETTER MEDICINE, BETTER ECONOMIC SENSE

- ➢ **Focus on early health rather than late disease**
- ➢ **It is better medicine to prevent disease early. e.g. treat cardiac disease at the onset of symptoms of high cholesterol, high blood pressure, etc.**

FACTS re NON- PREVENTIVE MEDICINE

- Currently 70-80% of healthcare resources are spent on advanced diseases
- 70 million baby boomers (age 50 y and older) are eligible for colon cancer screening. Fewer than half have complied
- The 5 year survival rate for colon cancer is 90% for localized cancer and 8% if the cancer has spread further in the body
- Breast cancer survival has improved dramatically as a result of routine mammograms

OH! WHAT A WONDERFUL WORLD!

- In our field this is true
- There are great opportunities to serve patients better through advances in diagnostic modalities and improved information technology
- The cost of routine testing has been reduced drastically (however genetic and molecular tests are very expensive)
- We will see better preventive medicine and personalized medicine

LET US CELEBRATE!

THANK YOU TO THE ASSOCIATION OF CLINICAL BIOCHEMISTS OF INDIA AND ESPECIALLY TO DRS. DANDEKAR AND ASHAVAID

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