SP100 The Practice of Pathology in the Twenty First Century – Achieving Relevance in a Tidal Wave of Change

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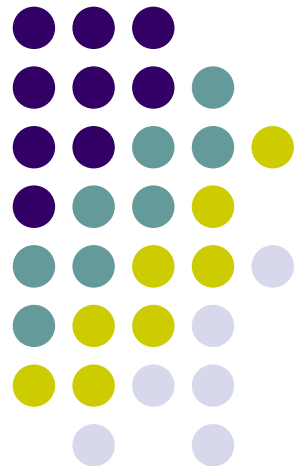
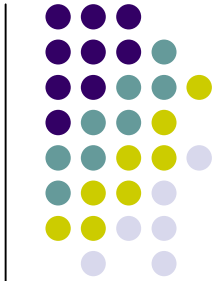
“The only way to predict the future is to create the future”

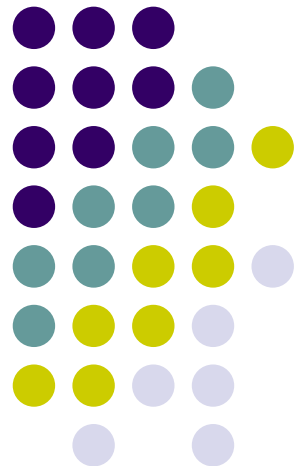


Urgency to Reconsider Path Forward as Pathologists



- Unabated increase in health care costs
- Compounding increase in new diagnostic technology
- Heightened interest in safety and quality of medical care
- Increased attention to decision making grounded in evidence based medicine

Unabated Increase in Health Care Costs



National Health Care Spending

- 1960 -- $28 billion
- 1970 -- $75 billion
- 1980 -- $255 billion
- 1990 -- $717 billion
- 2000 -- $1.36 trillion
- 2006 -- $2.16 trillion

National Health Care Spending

- 1960 – 5.2% GNP
- 1970 – 7.2%
- 1980 – 9.1%
- 1990 – 12.4%
- 2000 – 13.8%
- 2006 – 16.5%

Growth Factors

- Aging America
- 2007 – 30 million Americans over 65 (10%)
- 2030 – 72 million (20%)
- Raise health care spending by 25%

Growth Factors

- Evolving Technology
- 2007 -- $125 billion (7%)
- More people benefiting from technology (living longer with chronic disease)

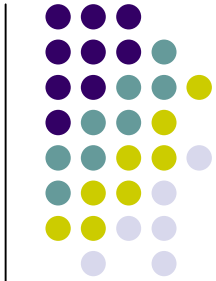
Projection

- 2015 – $4 trillion (20%)
- 2030 – 25%

Spending Base

- 32% Households
- 26% Private business
- 22% Federal government
- 17% State and local government
- YOU (2004 -- $6280 per person)

Are We Getting Our Money's Worth



- US – 15%
- Switzerland – 10.9%
- Germany – 10.7%
- Canada – 9.7%
- France – 9.5%

Metrics

- Access -- 45 million uninsured
- Infant mortality – 28th
- Adult longevity – good but no cigar
- Balance between preventive and end of life care out of kilter

RAND Health Study (2004)

- 4612 adults in 12 cities
- Evaluated 439 quality of care indicators for 30 indicators of disease prevention or treatment
- Good methodology for indicators – literature reviews and Delphi techniques
- Good methodology for evaluation – duplicate chart audits by trained nurses, supplemented by interviews

RAND Health Study

- Acute and chronic conditions; preventive care
- Screening, diagnosis, treatment, follow-up
- Participants received 55% of recommended care

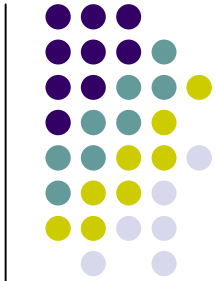
Lab Industry

- $30 to $50 billion
- 10 billion tests/year
- 33 tests, American
- 2.5% or less of the big picture

Lab Industry

- Disproportionate punch – 70 to 80% of medical decision making
- High investment rate – 35%
- Growing recognition as quality measures

New Technology -- FDA Vantage Point

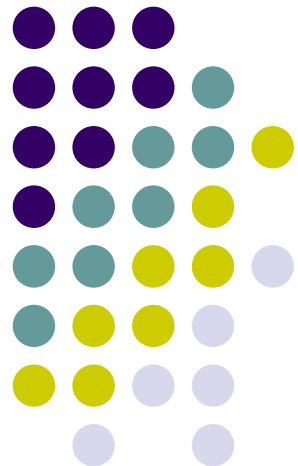


- Not an explosive growth but slow and steady incremental growth
- Improvements in existing technology
- Cutting edge new technology
- Like compound interest, growth although not exponential will be surprising

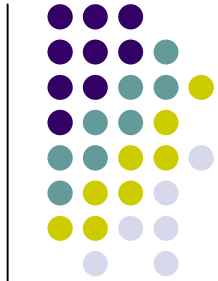
Industry Projections

- Overall 5.1% yearly growth over next 5 years from $15.2 to 19.5 billion
- Chemistry 4% growth ($ 6.7 billion)
- Immunoassays 5.3% ($ 5.3 billion)
- Nucleic acid tests 10.4% ($ 2.3 billion)

New Technology – Dual Edge Sword – costs and quality and costs

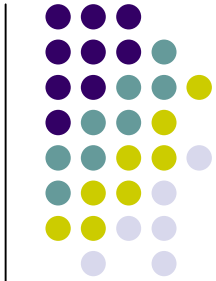


Laboratory Technology – Impact on Efficiency



- Biomarkers and tools for personalized medicine
- Biomarkers and tools for improved (faster and more accurate) diagnosis – infection based
- Improved diagnostic device design – better reagents, better instruments, better software
- Novel new technology

Biomarkers for Personalized Medicine



- April 14, 2003 – complete sequencing of human genome
- NIH Road Map
- FDA Critical Path
- HHS Personalized Medicine

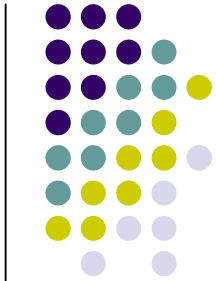
Biomarkers – Patient Based

- Tailored but old fashioned choices
- Diagnosis
- Prognosis
- Monitoring
- Treatment selection

Biomarker Tailored Treatment

- Preventive care – identification of at risk patients (genes, proteins, metabolites)
- More effective treatments – identification of patients likely to respond to a specific selected treatment (her 2 testing model)
- Safer treatments – identification of patients likely to exhibit adverse reactions (SAE consortium)

Biomarkers – Patient Based



- When drug becomes linked to diagnostic; drug effectiveness becomes a prisoner to the diagnostic (unsettling to colleagues in drugs)
- Laboratorians become drug doctors
- Not your father's Oldsmobile

Biomarkers

- More heat then light BUT there is real spirit here
- Does not have to be particularly exotic – troponin
- Can be exotic – expression array with IVDMIA features -- MammaPrint

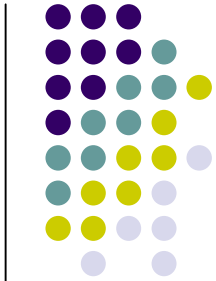
Multiple Marker Technology

- Swear by FDA – facile reviews
- Swear at FDA – over or under regulation
- Pipeline is busting
- More then 200 new tests from Alzheimer's Disease to transplant rejection

Biomarkers – Infection Based

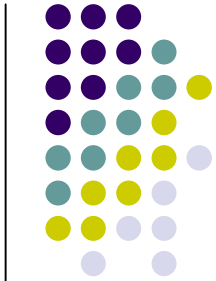
- Molecular diagnostics in search of microorganisms – chips and panels for broad detection of infectious diseases
- Don’t discount immunoassays – HIV to malaria – performance is amazing
- Profound impact on public health (ordinary, emerging, and biothreat pathogens)

Improved Diagnostic Device Design



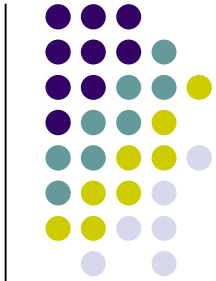
- Lab systems get better and better
- Central lab devices with quick performance on small samples with improving quality and quality control (EQC)
- Potential for point of care tests that do meet CLIA waiver requirements (POC)
- Potential for home use products

Improved Diagnostic Device Design



- Central lab devices with quick performance on small samples with improving quality and quality control (EQC)
- TAT should be easier target -- recalcitrant core overhead (transport, centrifugation, etc.)
- EQC will be a practice challenge – is it on the radar screen

Improved Diagnostic Device Design



- Point of care laboratory
- Core issue – performance versus access
- Evidence based medicine guidelines (2007) --the National Academy of Clinical Biochemistry
- Cost effectiveness studies

Value Added

- Activated partial thromboplastin time
- Prothrombin time
- Activated clotting time
- Arterial blood gases
- Group A strep
- Wet mounts for Trichimonas

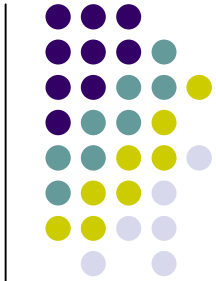
Not Well Advised

- Transcutaneous bilirubin
- Fructosamine
- Blood ketones
- Urine albumins
- Drugs of abuse
- Renal function tests

Jury's Out

- Cardiac biomarkers*
- Group B strep
- Influenza
- HIV
- BV
- hCG

Improved Diagnostic Device Design



- Potential for home use products – blood drawing and interpretation not technology are limiting factors
- Growth will be slow
- Consumer awareness and activism may not be so slow

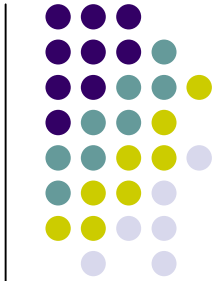
Lewandrowski (2003)

- “One result of the consumer phenomenon is that patients may learn of new diagnostic tests in the lay press or on the Internet…. Few physicians can resist the demands of a well-educated patient.”

Novel New Technologies

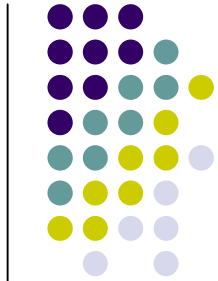
- Continuous glucose meters
- Breath tests
- Artificial intelligence or neural networks

Novel New Technologies



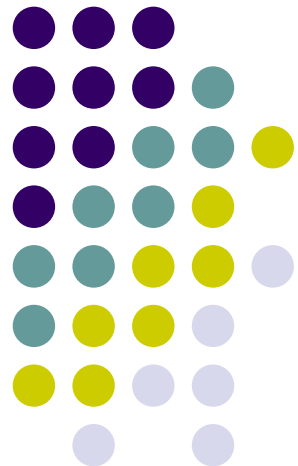
- Noninvasive testing -- extreme scenario; patient in a box, scan, diagnose
- Noninvasive testing – dramatic scenarios
  - MRI spectroscopy to predict prostate cancer biology
  - Light spectroscopy for pancreatic cancer

Growing Arsenal



- Challenge of menu selection
- Interpretative challenge
- Potential to be a cornerstone in change in medicine
- Lower costs – faster better decisions
- Improve quality – faster better decisions
- Lead to better outcomes

Heightened Interest in Safety and Quality



Patient Safety

- Not new issue (CAP 1946)
- Not new issue to medicine -- JCAHO
- Institute of Medicine – 1999

Patient Safety

- To Err is Human
- 98,000 deaths per year
- One million injuries
- Galvanized health care community
- 50% reduction in 5 years

Laboratory Interest -- dual

- Errors in testing – impact on patients
- Use of testing to measure quality of cares – defining, capturing, minimizing health care system errors

Errors in Testing

- Small but growing literature
- Lack of consistent language and methodologies
- Variable, method dependent reports on error rate

Errors in Testing

- Complaint based data -- .05%
- Total system audits -- .47%
- Process reviews (blood bank) -- 5%
- Process reviews – blinded secondary evaluation (anatomic pathology) – 4%

Errors in Testing

- Preanalytical – 41% to 68%
- Analytical – 4% to 13%
- Postanalytical – 18% to 55%

Errors in Testing

- Numbers are low – percentage (.05%)
- Numbers are high – volume effect (500,000 errors; 50,000 adverse events/year)
- Not competitive with best in other industries -- airlines

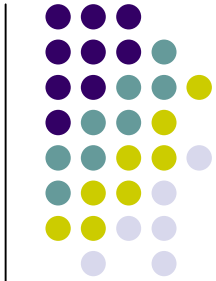
Errors in Testing -- Analytical

- Analytical performance overall is robust
- Labs have most control
- Labs have most regulation – CLIA, FDA for approved devices

Errors in Testing -- Analytical

- FDA tries to provide transparency
- www.fda.gov/cdrh/oivd

Errors in Testing -- Analytical



- Begs the issue of inherent quality of tests
- Good and getting better BUT
- Major problem is lack of standardization and traceability (commutability)
- To some extent routed in FDA law

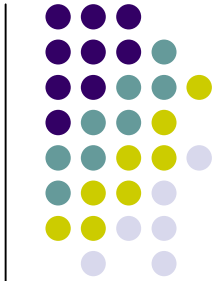
Errors in Testing

- FDA regulations allow for equivalence based (new products “substantially equivalent” to predicates)
- FDA regulations allow for safety and effectiveness but each on independent and non-connecting merits

Inherent Quality of Tests

- Lack of commutability
- PSA (all tumor markers)
- Troponin (all cardiac markers)
- Prothrombin times (all coagulation monitors)
- D-Dimers
- Glucose meters

Inherent Quality of Tests



- Interferences – specificity
- Measurement of free hormones or steroid hormones at low concentrations

Preanalytical Errors -- Traditional

- Obtaining appropriate clinical information
- Proper patient preparation
- Proper collection
- Proper sample handling

Preanalytical Errors – Customer Oriented

- Patient satisfaction
- Professional staff satisfaction
- User friendly order forms/formats
- Test collection access

Postanalytical Errors -- Traditional

- Verifying lab results
- Reporting values

Postanalytical Errors – Customer Oriented

- Communication
- Reporting of critical values
- Reporting of relevant reference ranges
- Interpretative guidelines
- Customer satisfaction

CAP Tools

- Proficiency testing
- I and A program
- Q-Probes
- Q-Tech
- Consensus conferences
- Protocol standards

CAP Tools: Three Formal Reviews

- Novis – 2004
- Stankovic -- 2004
- Howanitz – 2005
- Broad scope (total life cycle of testing)
- Variable findings
- Mimic literature

Three Outlines for Addressing Errors

- Novis – 2004
- Elin – 2004
- Howanitz – 2005

Novis Approach (2004): Detecting and Preventing Errors

- Very general
- Benchmark
- Two complementary general strategies

Prevent the Occurrence of Errors

- Educate healthcare workers
- Motivate healthcare workers
- Develop written policies and protocols
- Documentation
- Simplification

Accept Error

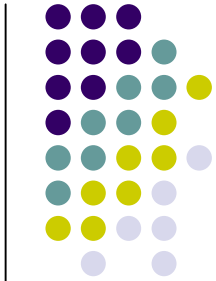
- Introduce redundancy
- Use of error detection systems
- Tools for continuous monitoring

Not Mutually Exclusive

Elin (2004) – Errors in Lab Medicine (General but Explicit)

- Establish CQI programs
- Have a user-friendly computer system that facilitates ordering
- Develop a quality wristband policy and use bar codes
- Establish quality programs for education and competency

Elin – General but Explicit Criteria



- Use automated systems where feasibility; favor those with error reduction systems
- Error detection in patient reports in all departments
- Policies and procedures for abnormal report reporting and consultation

Howanitz (2005): Practical Lessons for Safety

- **Entire Lab**
- Customer satisfaction
- Critical value reporting
- Patient identification
- Proficiency testing

Howanitz – Identify Critical Performance Measures

- **Two or more labs**
- Specimen rejection
- Turnaround times

Howanitz – Identify Critical Performance Measures

- **Lab specific**
- Blood product wastage
- Blood culture contamination

Not all inclusive

- Probe other areas

Broadest View

- Laboratory errors may be defined as any defect from ordering tests to reporting results and appropriately interpreting and reacting to these
- “Pre-pre” and “post-post” analytical error (Laposata 2007)

Broadest View

- Broad perception misuse of existing technology (overuse and under use)
- Problem in ordering and interpreting tests
- Well established perception with existing tests
- Likelihood to blossom with wild new tests
- Brain to brain information gap

Zieve (1966) – Misinterpretation of Lab Tests by Clinicians

- Over interpretation of test values
- Unfamiliarity with physiology factors affecting tests
- Unawareness of extraneous factors that influence tests
- Unawareness of distribution of normal
- Uncritical acceptance of published opinions

Eisenberg (1981) – Cost Containment and MD Behavior

- Education
- Peer review
- Administrative changes *
- Participation in decision making
- Penalties and rewards

Van Walraven (1998) – Do We Know Inappropriate Lab Use?

- Review of 137 papers (44 used)
- Implicit criteria – 11
- Explicit criteria – 33
- Range 4.5 to 90%
- Critical for good care and performance
- Need more vigorous methodology

Solomon (1998) – Techniques to Improve Use of Diagnostic Tests

- Review of 102 papers (49 used)
- Application of a 38 point methodology scale
- Evaluation of education, guideline development and use, audits, economic incentives
- Emphasis on behavior modification
- Need more vigorous methodology

Winkelman (1984) -- Misuse – Misdirected Target

- Methodologies are poor
- Piecing together facts is difficult
- Fixed costs tend to break the bank
- 10% decrease in tests – 4% decrease in costs
- 50% decrease in tests – 22% decrease in costs

Misuse -- Misdirected

- May be false gold – test cost is the tip of the ice burg
- Need to focus on the gold mine – patient decision making
- Cannot underestimate the harm in excess testing

Misuse

- Effect of false positive – Ulysses syndrome
- Labs using 2 SD reference ranges – 5%
- Iatrogenic anemia
- Delays in actual disease detection
- Emotional impact
- Work impact

Broadest View -- Kind

- Pathologists like to tend their own gardens
- Focus on technology of new (and old tests) and not use
- Connectivity between pathologists and user (both pre and post analytical) in general is suboptimal

Broadest View -- Blunt

- Abrogation of responsibility, broken chain from pathologist to patient
- Converted lab work into commodities not services
- Generate mentality labs are like cafeterias, subject to sub-contract, consolidation, use of prepackaged foods

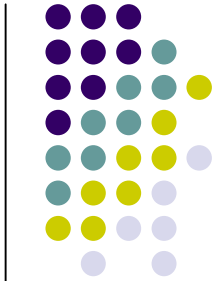
Misuse Issue: Under Use and Value

- Potassium
- Creatinine
- Troponin
- Tests for drug monitoring
- LFTs with Troglitazone (response to an FDA warning)

RAND Health Study (2004)

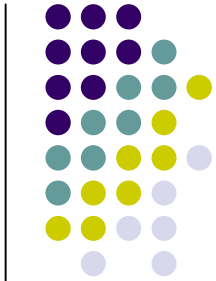
- Not exotic tests
- Theophylline – 62% under use
- Potassium – 22% under use
- FOBT – 72% under use
- HBA1C – 42% under use
- Lipid tests – 42% under use

Health Plan Employer Data and Information Set (HEDIS) (2004)



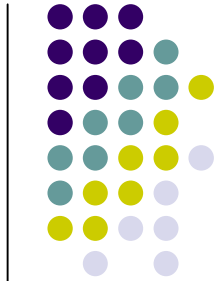
- National Committee for Quality Assurance
- Popular in managed care settings
- 26 effectiveness of care quality measures
- 6 are diagnostics

Health Plan Employer Data and Information Set



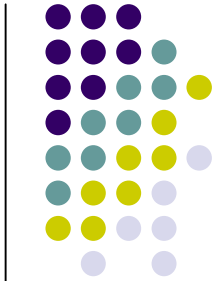
- Cholesterol management – 49% under use; $87 million
- FOBT or colonoscopy – 52% under use; $191 million
- HBA1C – 20% under use; $573 million

Cost Effectiveness



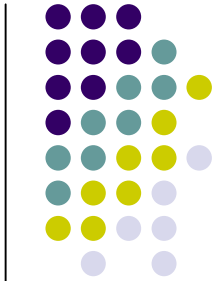
- Troponin
- Her 2/herceptin
- Point of care for infectious diseases – various modeling to elucidate test or treat decisions

Plebani (1999) – The Importance of Laboratory Reasoning



- The classical-technology approach
  - Objectives
  - Challenges
- The pathophysiology-based approach
  - Objectives
  - Challenges
- Both are needed

Hernandez (2003) -- Cost Effectiveness of Laboratory Testing

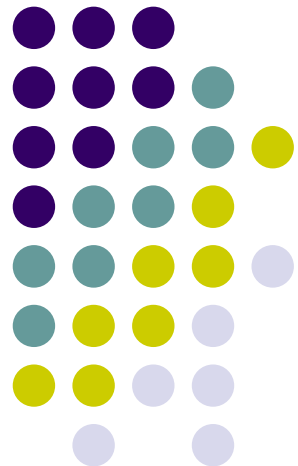


- Excellent road maps (cited)
- Paucity of high quality studies
- Pfister expository model for test assessment
  - Assay performance
  - Epidemiology of disease (prevalence and spectrum)
  - Cost of the test

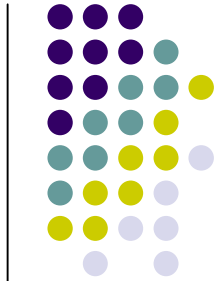
Cost Effectiveness of Laboratory Testing

- Differing physician practices
- Importance of total costs which can eclipse importance of test costs
- Need to understand patient outcomes

Evidence Based Medicine



Evidence Based Medicine

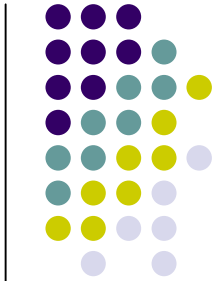


- Sackett definition (2001): The conscientious, explicit and judicious use of current best evidence in making decisions about the care of patients

Missing Ingredient – test value to system

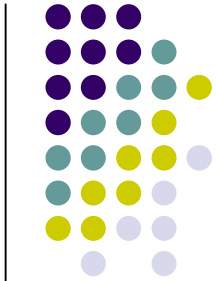
- Evidence based medicine
- Lab practice is highly empirical
- Seminal articles

Fryback and Thornbury (1991) – The Efficacy of Dx Imaging



- Technical efficacy (correct analytical signal)
- Diagnostic accuracy efficacy (correct clinical signal)
- Diagnostic thinking efficacy (impact on decision making
- Therapeutic efficacy (impact on therapy)
- Patient outcome efficacy (impact on outcome)
- Societal efficacy (public health good)

Reid (1995) – Use of Methodological Standards

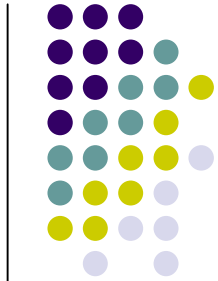


- Spectrum bias
- Subgroup analysis
- Workup bias
- Review bias
- Precision of results
- Indeterminate results
- Test reproducibility

FDA: Test Evaluation Not Easy

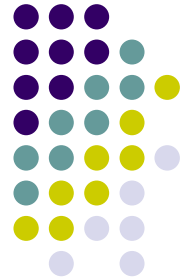
- Sampling bias
- Spectrum bias
- Verification bias
- Missing data
- Discrepancy resolution
- Identifying yardstick of truth (gold standard)

STARD Initiative (2003)



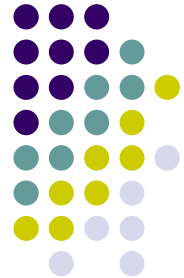
- 25 item checklist
- Abstract
- Introduction
- Methods
- Results
- Discussion

Formula – American Cancer Society (2005)



- There must be good evidence that each test or procedure recommended is medically effective
- The medical benefits must outweigh risks
- The cost must be reasonable compared with expected benefits
- The recommended actions must be practical and feasible

Marchevsky (2005) -- Approach to Testing



- Formulation of specific diagnostic question
- Search for specific scientific literature
- Critical appraisal of the evidence
- Incorporation of “best evidence” from several “reliable sources” with personal clinical experience for development of rules
- Evaluation of effectiveness/efficiency of recommendations

Wick (2005)– Evidence Based Principles and Practices In Path

- Explicit examples
- Sacred cows
- Magical thinking

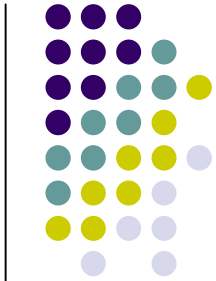
Knowledge is Power

- Who will make decisions
- Third party payers
- Architects of practice guidelines
- Health care providers
- Patients (advocates)
- Pathologists

Challenge to Pathologists # 1

- How to address lab quality
- Paradigm is work on EP 22 and 23
- Transfer of assignment of QC responsibility from government (CMS) to laboratorians
- Well grounded; challenge in the execution

EP 22 –Manufacturer's Risk Mitigation Information



- Document on product design
- Risk assessment
- Strengths of the product including built-in process or internal controls
- Information to understand strengths and weaknesses of test system at hand
- Proposed draft

EP 23– Lab QC Protocols

- Laboratory user document
- Assess unique lab needs based on stability of environment, competence of operators, performance needs of health care providers
- Match with information in EP 22
- Make informed QC decisions*
- EQC belongs to the lab (cost, quality, liability)
- Proposed draft

Challenge to Pathologists #2

- How to navigate new technology and help ensure proper use
- Companies always have reached out to clinicians to make end runs
- Now more then ever
- Reports use of esoteric tests (nature of tests changing fast) on the rise
- If you build it, they will come

Challenge to Pathologists

- Pathologists must keep up with technology
- Pathologists must become educators and gate keepers
- Pathologist must assert themselves as critical part of the diagnostic process in patient care
- Alternative option is to lose the farm*

Challenge to Pathologists #3

- When and how to support portable technology
- How to exploit in health care systems
- How to address competitively
- How to make laboratory selection choices

Role of Pathologist, Diverse but Overlapping Models

- Schwartz – 1992 (optimistic prescient vision)
- Laposato – 1994 (workman like recommendations)
- Plebani – 2002 (impassioned diatribe)
- Lewandrowksi – 2003 (enunciation of gatekeeper role)

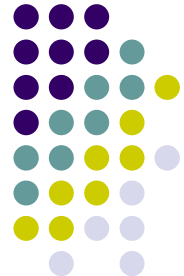
Schwarz (1992) – What Will the Pathologist be Doing in 2001?

- The pathologist must learn how to be flexible and how to adapt rapidly to marked changes in the work environment
- The pathologist must be an excellent communicator
- The pathologist must be a leader and know how to motivate people
- The pathologist must remain as a responsible educational link between clinical medicine and basic science

Schwarz - What Will the Pathologist be Doing in 2001?

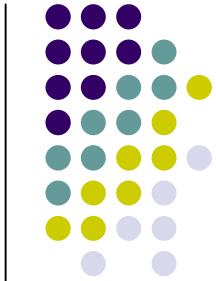
- The pathologist must love acquiring new knowledge and sharing new knowledge
- The pathologist must understand information systems
- The pathologists must be knowledgeable in the use of management tools and recognize their importance
- The pathologist must function in team or groups
- The pathologist must be a people person

Laposato (1994) -- What Many of Us Are Doing or Should Be Doing



- Provision of clinical information through microscopic review, interpretation of tests, evaluation of patients
- Control of clinical laboratory utilization through clinician initiated request or triggers of lab send-outs, unusual orders, or inappropriate orders
- Performance of quality assurance activities

Plebano (2002) – Charting the Course of Medical Laboratories

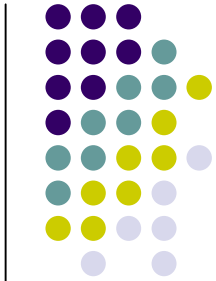


- Selection of methods based on quality specifications and practice needs
- Setting and monitoring total allowable error and measures for QC and QA
- Assessing role in improving system performance
- Performing regular clinical audits directed at improving outcomes

Plebano – Charting the Course of Medical Laboratories

- Adopting objective interpretation criteria
- Using patient –specific narrative interpretations
- Participating in the shift to preventive care
- Using practice based medicine for decision making to establish menu of tests

Lewandrowski (2003) –Managing Utilization of New Dx Tests



- Best interest of patient
- Actively solicit opinions of others
- Project a team-oriented approach
- Develop organizational skills
- Maintain and expand your fund of medical knowledge

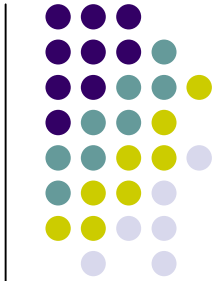
Lewandrowski – Managing Utilization of New Dx Tests

- Maintain persistence, execution and follow-through
- Be prepared to negotiate deals and seek win-win arrangements
- Learn how to close a deal
- Be humble. Admit when you are wrong or lack knowledge
- Good ideas are useless without execution

Good News for Pathologists

- Opportunity to apply unique knowledge
- Opportunity to apply unique intersection of information (multiple tests to laboratory)
- Opportunity to leverage two august traditions – anatomic and clinical pathology into a discipline in which the sum is greater then the parts
- Pathologists must leave their gardens and both metaphorically and literally go to the bedside

Bad News -- Everyone Is Interested



- Non-pathologists MD's (usually specialty based)
- PhD's (usually well trained in niche subjects and well versed in niche)
- Med techs, nurses, other health care professionals
- Businessmen usually with a bottom eye on the dollar but often with clever and interesting science and marketing
- Pathologists must be activists

Preparing For the Charge

- Institutions will need to be ready with programming (CAP is well positioned*)
- Educational programs will need to be attentive to menu of educational needs*
- Individuals will have to do what physicians are supposed to do – be perpetual learners and also leaders*

The Straight Facts

- IVD industry slow to promote value base for competitive reimbursement
- Pathologists slow to lead in use of lab tests and to demonstrate how lab tests can impact patient safety, total costs, and health care outcomes
- Pathology as science, art, political science!
- Exploit the skills that have made control of analytical processes so successful

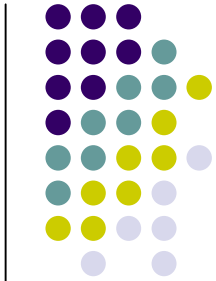
Frost-like View

“I shall be telling this with a sigh
Somewhere age and ages hence;
Two roads diverged in a wood and I ---
I took the one less traveled by
And that has made all the difference”

The Future is Ours

- CAP conference
- CAP tools
- FDA tools
- CLSI tools
- Flourishing literature

Lundberg (1998) -- The Need for an Outcomes Research Agenda



- "The real reasons for laboratory testing should be to improve the outcome for the patient's or the public's health. The time has come to develop a solid *research* agenda to measure and monitor these vitally important outcomes and to change practices when indicated by the results."