Pathology at the Foundation and Frontier of cancer care

By
Professor Dr. Looi Lai Meng
MBBS, MD, MIAC, FRCPath, FRCPA, FAMM, FASc, FAMS
Professor of Pathology, University of Malaya
National Distinguished Professor
Past-President, WASPaLM

2018 WORLD CANCER CONGRESS
Kuala Lumpur, Malaysia
1-4 October 2018
Disclosure

- No conflict of interest
- No commercial sponsorship
- Studies and papers cited are duly acknowledged
2018 Lancet Series on Global Pathology

Pathology and laboratory medicine in low-income and middle-income countries

Access to pathology and laboratory medicine services: a crucial gap

Michael L. Wilson, Kenneth A Fleming*, Modupe A Kuti, La Meng Looi, Nestor Lolo, Kun Liu

www.thelancet.com Published online March 15, 2018 http://dx.doi.org/10.1016/S0140-6736(18)30458-6
CONTRIBUTION OF PATHOLOGY & LABORATORY MEDICINE TO PATIENT CARE

**Screening**
- Early detection of risk factors and premorbid conditions

**Diagnosis**
- Classification and subtyping
- Prognostic and predictive indicators

**Monitoring**
- Adequacy of treatment
- Recurrence of disease
- Complications

**Research**
- Aetiology
- Disease pathways
- New biomarkers
- Clinical trials

“As is your pathology, so is your Medicine”

- Sir William Osler-

Cancer is impossible to treat accurately unless one knows the pathological diagnosis.
Breast cancer is heterogenous
Histological typing has prognostic significance

<table>
<thead>
<tr>
<th>Type</th>
<th>5 yr survival</th>
<th>30 yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubular/cribriform; Papillary</td>
<td>90-95%</td>
<td>65-75%</td>
</tr>
<tr>
<td>Mucinous; medullary</td>
<td>70-80%</td>
<td>60%</td>
</tr>
<tr>
<td>Lobular</td>
<td>70-80%</td>
<td>35%</td>
</tr>
<tr>
<td>Ductal, NST</td>
<td>60%</td>
<td>30%</td>
</tr>
</tbody>
</table>

**Worse prognosis:** Signet ring, Metaplastic, Lipid-rich
Era of Personalised Medicine

- “One size does not fit all”
  - Biological variation
  - Inherent vs adaptive
- All treatment have costs & side-effects
  - Justified only if good chance of response
  - Reduce cost and resources
  - Reduce treatment failure
  - Avoid drug toxicity
Pathology/molecular profiling is now widely used to stratify breast cancer patients for targeted therapy

- Based on oestrogen and progesterone receptor expressions and HER2 oncogene amplification
- Immunohistochemistry & FISH
- Gene expression profiling
Molecular subtypes of breast cancer by biomarker expression

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Biomarker profile</th>
<th>Prevalence</th>
<th>Therapeutic options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A</td>
<td>ER+ and/or PR+, HER2-, Ki-67 low</td>
<td>40%</td>
<td>Endocrine therapy (tamoxifen)</td>
</tr>
<tr>
<td>Luminal B</td>
<td>ER+ and/or PR+, HER2+ (or HER2- with high Ki67)</td>
<td>20%</td>
<td>Endocrine therapy (tamoxifen) +/- Trastuzumab (Herceptin)</td>
</tr>
<tr>
<td>HER-2 type</td>
<td>ER-, PR-, HER2+</td>
<td>10-15%</td>
<td>Trastuzumab (Herceptin)</td>
</tr>
<tr>
<td>Triple negative/basal-like</td>
<td>ER-, PR-, HER2-</td>
<td>15-20%</td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>
Gastrointestinal Stromal Tumour (GIST)

- A unique stromal tumour of GIT characterised by IHC cytoplasmic positivity for CD117 (c-KIT)
- ~90% GIST have KIT or PDGFRA “gain-in-function” mutation
- Imatinib is a specific inhibitor of KIT tyrosine kinase activity and blocks KIT-mediated downstream signaling\(^2\)
- Selective inhibition of the KIT and PDGFR\(\alpha\) RTKs with imatinib effective for treating GIST
  - Analogous to CML

CML, chronic myeloid leukemia; RTKs, receptor tyrosine kinases;
Non-small cell lung cancer: Targeted therapy

- Lung cancer in non-smokers
  - Distinctly different from smoking-related NSCLC
    - Lower K-ras mutations
    - Higher EGFR mutations

- Genetic profiling of NSCLC are useful in selecting patients for targeted therapy
  - EGFR mutation
    - Higher efficacy with EGFR inhibitors (e.g. gefitinib)
  - ALK gene rearrangement
    - Higher efficacy with anti-ALK (e.g. Crizotinib)
Targeting colorectal cancers with EGFR overexpression for treatment with anti-EGFR monoclonal antibodies (cetuximab and panitumumab)

KRAS oncogene mutations in colorectal carcinoma

- Predictor of resistance to EGFR inhibitor therapy which are currently used for metastatic colorectal cancer.
- Associated with a worse prognosis.


Key points

- Accurate cancer diagnosis is crucial for appropriate treatment and outcome
- We are in the era of personalised medicine
- Profiling
  - Diagnostic: established
  - Prognostic: established
  - Predictive (targeted therapy): current challenge
- Beyond profiling: new approaches and research
Acute shortage of anatomical pathologists in LMICs

- SSA 1:1,100,000
- China: 1:134,517
- Myanmar: 1:170,000
- Vietnam: 1:250,000
- Malaysia: 1:55,000

Pathology and laboratory medicine (PALM) services are cross-cutting, intersectoral, and provide the foundation for safe, effective, and equitable health-care delivery, population health, and global health security.

Access to PALM services in low-income and middle-income countries is severely inadequate and inequitable.

The Sustainable Development Goals and universal health coverage cannot be achieved without PALM services.
Key messages

- Investment in human resources will be crucial to overcome the gap in access to quality pathology and laboratory medicine (P ALM) services.
- Information technology and point-of-care testing cannot compensate for weak health-care systems.
- A P ALM delivery package within an integrated network of tiered laboratories can help address the problems of access to P ALM services in low-income and middle-income countries.
- Research to map P ALM challenges more accurately and to determine optimal solutions is urgently needed.
Telepathology

- Telepathology has the potential to address the problem of insufficient on-the-ground anatomic pathology expertise.
- Allow remote users to provide anatomical pathology diagnoses by analyzing digital images or dynamically examining a slide in real time.
- Support remote tumour board discussion