The role of a Laboratory Specialist
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Chemical Pathologist
St Vincent’s University Hospital, Ireland
School of Medicine, University College Dublin

THE BRITISH ISLES

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- Blarney Castle is famous for its stone, which is traditionally believed to have the power to bestow eloquence on all those who kiss it.
- The term "Blarney" was introduced into the English language by Elizabeth I of England and is defined as "pleasant talk, intending to deceive without offending".
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DISCLOSURE

- I have many roles
  - St Vincent’s University Hospital
  - School of Medicine University College Dublin
  - Faculty of Pathologists Ireland
  - Association of Clinical Pathologists
  - UEMS
- The views are my own unless stated otherwise

DISCLOSURE

- I have an intercalated BSc and a MB
- Chemical Pathologist is a title that only medics can use
- I have completed Higher Specialist Training in Laboratory Medicine / FRCPath exams in Chemical Pathology
- I have never done any specialist Physician exams
UK & Republic of Ireland

- Geographically: Border each other
- Historically: Hundreds of years of shared history
- Main language: English
- Legal system: Adversarial, non codified; previously common
- Shared full voting entitlements, more than in the EU
- Passport agreement independent of the EU
- Tax agreement independent of the EU

Medical Royal Colleges

- The first establishment of what became a Medical Royal College was the Guild of Surgeons in the 14th century
- Royal charters were awarded
  - The Royal College of Surgeons of Edinburgh 1506
  - The Royal College of Physicians of Ireland in 1654
  - The Royal College of Surgeons of England 1800
- The Royal College of Pathologists was founded in 1962
Different Groups with in labs in UK & Ireland

Different Groups in UK
- Medical
- Biomedical Scientist
- Clinical Scientist
- Medical Laboratory Aid

Different Groups in Ireland
- Medical
- Clinical Biochemist
- Laboratory Aid
- Medical Scientist

State Registered Groups in UK
- Medical
- Biomedical Scientist

State Registered Groups in Ireland
- Medical

Some Laboratory Proficiencies: UK

<table>
<thead>
<tr>
<th>Proficiencies</th>
<th>Biomedical Scientist</th>
<th>Clinical Scientist</th>
<th>Chemical Pathologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Be able to identify the clinical decision which the test or intervention will affect</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Be able to interpret data and provide diagnostic and therapeutic opinions, including any further action which the individual directly responsible for the care of the patient or service user should take</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Be able to develop an investigation strategy which takes account of all the relevant clinical and other relevant information available</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Be able to manage a laboratory and its personnel</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Be able to use quality control and quality assurance techniques, including decision rules and cut-off values</td>
<td>Biomedical Scientist</td>
<td>Biomedical Scientist</td>
<td>Biomedical Scientist</td>
</tr>
<tr>
<td>Be able to use quality control and quality assurance techniques and data transfer</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Understand the specific clinical situations relevant to the service user receiving the service</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Understand the specific clinical situations relevant to the service user taking the test</td>
<td>Not required</td>
<td>Required</td>
<td>Required</td>
</tr>
</tbody>
</table>
STATE REGISTERED GROUPS IN UK

Clinical Biochemistry

Medical

Clinical Scientist

BMS

STATE REGISTERED GROUPS IN UK

Significant overlap between medical and clinical scientists

Differences exist

Professional boundaries are important – clinical governance

STATE REGISTERED GROUPS IN UK

Significant Differences Exist

Professional boundaries are important – clinical governance

STATE REGISTERED GROUPS IN UK

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Chemical Pathologists

- Patient services
  - Out-Patient Clinics
  - Ward Consultations
  - Ward Rounds
  - Clinical Trials

Training

- Capability is what you can do with training
  - I am capable of becoming a neurosurgeon
- Competence is what you actually do after training
  - Despite being a doctor, I have not had the training to become a neurosurgeon, so I unsurprisingly do not have the expected competencies of a neurosurgeon
- Competence is not constant – you need to keep your knowledge and skills up to date

Medical Training

- Medical Degree
  - a lot of patient interaction in UK & Ireland
- Provisional registration year
- Basic Specialist Training
  - With or without acute physician exam
- Higher Specialist Training

Medical Training

- Higher Specialist Training includes
  - Curriculum set by RCP path/Faculty of Pathology - clinics
  - Training programmes with fixed terms of 5+ years
  - Minimum specialist training for registration - 5 years
  - Appraisal (informal) - two per year
  - Annual Individual review (formal)
  - Regular review of training centres
  - Work place based assessment
  - RCP path examinations: Knowledge and skill based
    - Written, practical, data handling, clinical cases, research & oral exams
  - External review of individual training with 1 year to go to ensure training programme followed

Medical Training

- Clinical areas – all depend on lab results
  - Lipids / CVD risk assessment
  - Hypertension
  - Diabetes
  - Obesity
  - Endocrine
  - Nutrition especially parenteral
  - Metabolic Bone Disease
  - Renal Stones
  - Adult inborn errors of metabolism
  - Porphyria

Medical Training

- Different models
  - Service run by a lab consultant / team
  - Service run by a non lab consultant / team
  - Service run in a different hospital / region outside of rotation
  - Chemical Pathology is a small speciality
  - Role depended on
    - Individual training
    - Local requirements
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My experience

- Lipids / CVD risk assessment clinic
- Eating Disorder Nutrition clinic

My experience

- Lipids / CVD risk assessment clinic
  - Regular clinic exposure since I first did Basic Specialist Training
    - Atorvastatin was coming to the market
    - Before Rosuvastatin and Ezetimibe came to the market

Read the guidance

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of European Association for Cardiovascular Prevention & Rehabilitation

- Authors/Task Force Members: Šárka Reiner (ECE Chairperson), Czechia, Alberto L. Carrascosa (ECS Chairperson), Spain, Guy De Becker (Belgium), Jan Gretemans (Belgium), Marja-Miia Tikkkanen (Finland), Ola Nilsson (Sweden), Svetlan Agradski (Ukraine), Eduardo Antonio da Silva, M. John Chapman (France), Paul Durrington (UK), Saeed Bakhsh (Turkey), Johan Hakansson (UK), Robert Hobbs (UK), John Kjekshus (Norway), Pasquale Perrenoud Francini (Italy), Gabrielle Riccardi (Italy), Robert F. Sterrey (UK), David Wood (UK).

Read the guidance

JBS3 Report

The report is published to the report are consensus recommendations and are a collaborative effort from the British Cardiovascular Society (BCS) and the British Heart Foundation (BHF). Recommendations are developed separately for men and women. The report was written for GPs and professionals to help guide what was right and wrong in preventing cardiovascular disease. Recommendations are an evolution of earlier reports and are based on the latest evidence.

Familial hypercholesterolaemia: identification and management

Search NICE

- Familial hypercholesterolaemia: identification and management
  - Published June 2006
  - Last updated November 2017
  - Version 3
  - Status: Under review

NICE National Institute for Health and Care Excellence
Know the Evidence Base

- Historical aspects
- Risk Assessment
- Communication
- Lifestyle modification
- Drug treatment
- Follow up

Primary

Secondary

Relative Risk = 0.84 (0.70-1.00), p=0.048

MIRACL: Benefits of Intensive Lipid Lowering
- Relative Event Rate Reduction in Primary Endpoint

Comparative Safety Profile

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=1548)</th>
<th>Atorvastatin (n=1538)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated liver transaminases to &gt;3xULN</td>
<td>0.6%</td>
<td>2.5% (p&lt;0.001)</td>
</tr>
<tr>
<td>Myositis</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Any serious adverse event</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

PROVE IT (Pravastatin Or Atorvastatin Evaluation and Infection Therapy)

- Do the benefits of "intensive" LDL-C lowering to ~1.8mmol/L with 80mg atorvastatin achieve a greater reduction in clinical events than "standard" LDL-C lowering to ~2.6mmol/L with 40mg pravastatin

Changes from (Post-ACS) Baseline in Median LDL-C

Benefits of intensive Lipid Lowering on All-Cause Death or Major CV Events (Primary Endpoint at 2 Years)
Tolerability and Safety Profile

<table>
<thead>
<tr>
<th>Reason for Discontinuation</th>
<th>Atorvastatin 80mg</th>
<th>Pravastatin 40mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation for AE, patient preference or other reasons</td>
<td>30.4%</td>
<td>33.0%</td>
</tr>
<tr>
<td>Discontinuation for elevation</td>
<td>2.4%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>ALT ≥ 3 ULN</td>
<td>3.3%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Dose halving for AE or raised LFT</td>
<td>1.9%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

P-value

- 0.11
- 0.23
- N/A
- <0.001
- 0.20

Cannon CP et al. NEJM 2004; 350(9)

HPS Numbers

- Screened: 63,803
- Pre-randomisation:
  - 4 week placebo: 32,145
  - 4-6 week active phase: 23,974
  - Randomization to study: 20,536

- 3438 or 14.34% of patients who met the study criteria and had no contraindications to being on simvastatin 40 mg (CK, LFTs, etc) did not continue.


HPS Numbers

- Cancer diagnosed during run-in: 28
- MI, CVA or hospitalisation for angina during run-in: 94
- Lipid-lowering drug started: 271
- New unexplained muscle symptoms: 531
- Other adverse event: 161
- Patient wishes or long-term adherence in doubt: 2092
- Patient physician discouraged participation: 36
- Other reasons: 135
- Any of the above: 3438

PRIMO Study

- An observational study of muscular symptoms
- Unselected population of 7924 hyperlipidemic patients receiving statin therapy in a usual care outpatient setting in France
- Patients treated with the penultimate or ultimate dose of statins
- Muscular symptoms were reported by 10.5%. Median time of onset of 1 month with 15% 8 months after initiation of statin therapy
- Multivariate analysis revealed predictors of muscular symptoms
  - A personal history of muscle pain during lipid-lowering therapy (OR 10.12; 95% CI 8.23–12.45)
  - Unexplained cramps (OR 4.14; 95% CI 3.46–4.95)
  - A history of CK elevation (OR 2.04; 95% CI 1.56–2.68)


PRIMO Study

- 25% continuous, 73% intermittent (several minutes or hours)
- Discomfort was widespread in 69.1% with 24.2% reporting pain “all over”
- <4% used analgesics for pain relief
- Muscular pain in these patients
  - Prevented even moderate exertion during everyday activities in 38%
  - 4% were confined to bed or unable to work
- Muscle Symptoms
  - Fluvastatin XL: 5.1% p<0.001 w.r.t. Pravastatin high dose
  - Pravastatin (high dose): 10.9%
  - Atorvastatin: 14.9% p=0.04 w.r.t. Pravastatin high dose
  - Simvastatin: 18.2% p<0.001 w.r.t. Pravastatin high dose


IRISH STOUT

Cork’s finest stouts proud to be working together

Know the relevant Signs & Symptoms

Know the guidance

Diagnostic criteria

1. Simon Broome diagnostic criteria for index individuals (proband)

2. Gender- and age-specific LDL-C criteria for the diagnosis of FH in relatives of a person with FH

Know the guidance

Nondiabetic Women
Non-smoker
Age under 50 years

Know the guidance

Table 1. Lipoprotein levels to be used as diagnostic criteria for the index individual

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>LDL-C (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>130-160</td>
</tr>
<tr>
<td>Children</td>
<td>100-130</td>
</tr>
</tbody>
</table>

Irish Recommendations for lipid testing and reporting

- It is recommended that the risk of Familial Hypercholesterolaemia is highlighted for calculated LDL-cholesterol concentrations $\geq$ 5.0 mmol/L
  - By means of an automated laboratory comment, e.g., “Significantly elevated LDL-cholesterol. If there is a personal or family history of premature vascular disease then this patient may have Familial Hypercholesterolaemia”
  - Other process such as discussion with requester

Use the guidance

| Table 1 Cholesterol levels to be used as diagnostic criteria for the index individual |
|---------------------------------|-----------------|-----------------|
| Child/young person              | Total cholesterol | LDL-C           |
| Adults                          | $\geq$ 6.5 mmol/L | $\geq$ 4.0 mmol/L |
| Levels within pre-treatment or highest on treatment |

Use the guidance

Note: gender- and age-specific LDL-C criteria for the diagnosis of FH in relatives of a person with FH.
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Criticate the guidance

Serum Cholesterol Levels in Men*

Framingham Heart Study

*During the 15 years of study. Entry ages 30–40 years.
Adapted from Castelli WP et al., Circulation 1988;77:772–778.
Increased HDL and Reduced CHD Incidence

Framingham Study

Relative risk of CHD

Adapted from Kannel WB. Status of risk factors and their considerations in anti-hypertensive therapy. Am J Cardiol 1987;59:80A-90A.

<table>
<thead>
<tr>
<th>LDL (mg/dl)</th>
<th>LDL (mmol/L)</th>
<th>HDL (mg/dl)</th>
<th>HDL (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>220</td>
<td>5.7</td>
<td>25</td>
<td>0.65</td>
</tr>
<tr>
<td>160</td>
<td>4.1</td>
<td>35</td>
<td>0.90</td>
</tr>
<tr>
<td>100</td>
<td>2.6</td>
<td>45</td>
<td>1.16</td>
</tr>
<tr>
<td>50</td>
<td>1.3</td>
<td>55</td>
<td>1.42</td>
</tr>
</tbody>
</table>

Criticise the guidance

- Use your laboratory background
- Biological variation
- Use your medical training
- Pharmacology

Make the guidance

- Use your lab background
  - Biological variation
- Use your medical training
  - Pharmacology
**Rule of 5 & Rule of 7**

- A doubling of each statin lowers Total Cholesterol an additional 5%
- A doubling of each statin lowers LDL-C an additional 7%
- Doubling of side effects

---

**LDL-C reduction and statins**

**LDL-C Mean change (%) from baseline at week 6**

- Rosuvastatin
- Atorvastatin
- Simvastatin
- Pravastatin

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**LDL-C reduction: Adding Ezetimibe**

**LDL-C Mean change (%) from baseline at week 6**

- Rosuvastatin
- Atorvastatin
- Simvastatin
- Pravastatin

---

**Risk: Benefit – Muscle**

- CK >10 × ULN frequency by % LDL-C reduction

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**Risk: Benefit – Liver**

- Persistent ALT >3 × ULN: Frequency by LDL-C reduction

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*References*:

Brewer HB. Am J Cardiol 2003;92(Suppl):23K–29K

**Show your knowledge**

- **Rule of 5 & Rule of 7**
- A doubling of each statin lowers Total Cholesterol an additional 5%
- A doubling of each statin lowers LDL-C an additional 7%
- Doubling of side effects

---

*Note*: This document contains graphical representations of statistical data and clinical information related to lipid-lowering medications and their potential side effects. The statistics presented are based on clinical trials and meta-analysis studies.
My experience

- Eating Disorder Nutrition clinic

Eating Disorder Nutrition clinic
- It started with me being invited to talk about lab tests
  - Ferritin is the best marker of low Iron status
  - Total CO2 / Bicarbonate is the best marker of low Potassium status
  - Urine Chloride goes down in vomiting
  - Fluid assessment also requires urine, Osmolality also important

Eating Disorder Nutrition clinic
- The Psychiatrist and Team (Nurses, Dietitian & Psychologist) all realised that they knew less than I did
  - The usual tests were normal in patients who were clearly not normal
  - I made it clear that I did not have my Physician exams

Eating Disorder Nutrition clinic
- Back to basics
  - History
  - Exam
  - Relevant lab serum and urine tests
  - Relevant non lab tests
    - ECG
    - DXA Scan
    - BP and Heart Rate

Eating Disorder Nutrition clinic
- I saw all patients with a team member
  - History largely provided to me by the team
  - Examination
    - Salivary gland enlargement
    - Muscle wastage – hands
    - Heart Rate, Postural BPs
Eating Disorder Nutrition clinic

- Standardised serum and urine profile
- The lab tests were reviewed before I saw the patient
  - Amylase
  - Hypokalaemia and/or metabolic acidosis
  - Low urinary Chloride
  - Low Vitamin D
  - Low zinc adjusted for albumin

Eating Disorder Nutrition clinic

- Not a well developed area of medicine
- But I knew more than the GPs and many individual consultants/specialists
- My input was appreciated and trusted
- The team and I co-ordinated the care
- I oversaw the referral of the patients to specialists
- We made it easier for the specialists & GPs

Conclusions

- Previous patient exposure is a major help
  - Join other teams
  - Change the curriculum
- Chronic Disease Management
  - Common themes, e.g., adherence
  - Communication with the patient is important
  - Psychology
  - Emphasis

Conclusions

- Healthcare systems differ – different opportunities
- I did not compete with others
  - Niches develop – use your lab interests - use reflex comments or gather data using the LIMS
  - Others may be too busy / not interested
  - Others happy to have assistance