Edinburgh International Conference of Medicine

Past, Present & Future

#PPFEd16
www.pastpresentfuture2016.org
Recent History of Clinical Endocrinology

Professor John S Bevan
Aberdeen Royal Infirmary & Aberdeen University
Past, Present & Future...

“The division between past, present and future doesn’t mean anything, and has only the value of an illusion, tenacious as it may be”

Albert Einstein (1879-1955)
<table>
<thead>
<tr>
<th>Endocrinology speakers</th>
<th>MB Graduation</th>
<th>Profile</th>
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<tbody>
<tr>
<td>Peter Trainer</td>
<td>1983 Edinburgh</td>
<td>NHS Clinical Endocrinologist &amp; Researcher: GH action <em>in vivo</em> - ‘blocking the GH receptor’</td>
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Endocrinology: Past (History of...)

Personalised History of Endocrinology from 1978...
(only the briefest mention of more ancient glandular medicine)

1978-2015 = good time to be a clinical endocrinologist!
Advances in Endocrinology

- Hormone measurement
- Imaging endocrine glands
- Medical therapies
- Minimally-invasive endocrine surgery
- Endocrine networks: local, UK & international
- ‘Information Revolution’
- Specialist endocrine nursing
We stand on the shoulders of giants...

‘Father’ of Clinical Endocrinology

**Thomas Addison** (MB Edinburgh, 1812)

First physician to recognise an association between a diseased endocrine organ and a defined clinical syndrome (‘Disease of Supra-Renal Capsules’, 1855)

First ‘Practising Endocrine Physician’

**George R. Murray**

‘A note on the treatment of myxoedema by hypodermic injections of an extract of the thyroid gland of a sheep’ (BMJ, 1891)

The ‘Complete’ Physician

**Sir William Osler**

One of the first to treat Addison’s disease with a glycerine extract of pig adrenal gland (IMM, 1896)
Edinburgh faces from the past...three pituitary cases

- **Prolactinoma**
  - Primary treatment: Transcranial surgery

- **Acromegaly**
  - Primary treatment: Radiotherapy

- **Functionless pituitary adenoma**
  - Primary treatment: Transcranial surgery
Large pituitary tumour

Aims of Management

- Control hormonal hypersecretion
- Preserve pituitary function
- Relieve pressure effects
- Restore normal health prospects
Edinburgh 1979: Case 1

- Serum prolactin 157,000 mU/l (N<300)
- Transfrontal craniotomy
- Unable to work as a taxi driver
- Post-operative PRL 30,000 mU/l
- Bromocriptine
- External radiotherapy
- Irreversible hypopituitarism
Radioimmunoassay: enabled measurement of hormones in biological fluids ($10^{-9}$ to $10^{-13} \text{M}$)

**Rosalyn Yalow (1921-2011)**
- Insulin radioimmunoassay: 1960
- Nobel Laureate: 1977

**Prolactin**

1971: characterised as a hormone distinct from growth hormone

1971-73: first PRL radioimmunoassays

1973-77: early clinical studies of hyperprolactinaemia

1977: protein sequenced

1981: gene cloned
Prolactin Radioimmunoassay
(Oxford 1984)

- Slow procedure: batching & 48h assay
- Labour intensive: manual pipetting
- Required fresh $^{131}$I-prolactin production every 10-12w
- Multiple molecular forms of PRL

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Standard curve

Radio-iodination

Bevan JS – MD, 1987
REDUCTION IN SIZE OF A PITUITARY TUMOR BY BROMOCRIPTINE THERAPY

Alan M. McGregor, M.A., M.B., M.R.C.P.,
Maurice F. Scanlon, B.Sc., M.B., M.R.C.P.,
Keith Hall, M.B., F.R.C.R., D.M.R.D.,
David B. Cook, Ph.D.,
and Reginald Hall, B.Sc., M.D., F.R.C.P.

(NEJM (1979), 300: 291-293)
An early series of primary dopamine agonist therapy (1979)

Effects of bromocriptine on pituitary tumour size

A M McGregor, M F Scanlon, R Hall, K Hall

British Medical Journal, 1979, 2, 700-703

Metrizamide cisternogram before (a) and three months after (b) starting treatment with bromocriptine in case 4. The pituitary fossa is slightly enlarged and does not change. In (a) the diaphragma sellae is in its normal position (arrow), but in (b) it has dropped down into the fossa (arrowhead), indicating the development of a partial “empty sella” owing to tumour regression.
Prolactinoma shrinkage with bromocriptine

Bromocriptine treatment (wks)

% original tumour volume

Bevan JS et al., Clin Endocrinol (1987) 26, 541
World’s first MRI scanner

Aberdeen Royal Infirmary
Mark I Scanner
1000 patients
(1980-1983)
MRI – a major advance

0

3m

12m

60m (cabergoline Rx for prolactinoma)
Edinburgh 1979: Case 2

Acromegaly
- Radiotherapy 1968
- Hypopituitary
- GH still 8 µg/l (target <1)
- GH 4 µg/l on Bromocriptine 20mg
- No other medical options
- No IGF-1
- No MRI
Transsphenoidal surgery for acromegaly
Operating Microscope vs. Endoscope

Bevan JS, Acromegaly Consensus Conference, 2011
Medical therapy: Somatostatin Analogues (1980s)

16 patients
SC octreotide (no depot SA available)
Only 2/16 shrank (no MRI available)
Medical therapy: **depot somatostatin analogues**

**SC/LAR Octreotidetide**
Bevan JS et al.,
JCEM 2002

**Depot Lanreotide**
Caron P et al.,
JCEM 2014
Edinburgh 1979: Case 3

- Chiasmal compression
- PRL 600 mU/l (2xN)
- Urgent craniotomy
- No MRI for F/U
- ‘Routine’ XRT
- Testosterone replacement unsatisfactory
- No GH replacement
Non-functioning tumours: early DA experience

Bromocriptine treatment (wks)

%TV

0 10 20 30 40 50 60 70 80 90 100

Bevan JS et al.,
CEN 1987, Endocrine Rev 1992
Dopamine receptors in NFT cell membranes

Bevan JS & Burke CW, Clin Endocrinol (1986) 25, 561
NFT Remnant: Dopamine agonist or Radiotherapy?

Greenman, 2005  
Gittoes, 1998
<table>
<thead>
<tr>
<th>Hormone Replacement Therapies</th>
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<td><strong>1970s and 1980s</strong></td>
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<tr>
<td><strong>Glucocorticoid</strong></td>
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<td><strong>Thyroid hormone</strong></td>
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<td><strong>Testosterone</strong></td>
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<td><strong>Growth hormone</strong></td>
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Recent Improvements in Delivery & Standards of Endocrine Care
Collaborative networks

- **Local**: multidisciplinary teams (MDTs in pituitary, thyroid cancer, NET, adrenal)
- **National**: research/audit networks, peer review, standards of care
- **International**: research into rare diseases, clinical guidelines
The UK Acromegaly Registry (est. 1997) contains 3,298 patients, estimated to contain 86% of UK patients with acromegaly.

16 centres with <80 (total = 590)

- Barts, 345
- Birmingham, 298
- Oxford, 220
- Sheffield, 205
- Belfast, 177
- Christie, 177
- Edinburgh, 173
- Stoke, 160
- Cardiff, 168
- Newcastle, 144
- Leeds, 117
- Liverpool, 94
- Cambridge, 103
- Leicester, 104
- Aberdeen, 90

Peer-reviewed papers on outcomes after:
- XRT
- Surgery
- Medical therapies
International collaborations

A Consensus on Criteria for Cure of Acromegaly


Department of Medical and Surgical Sciences (A.G.), University of Brescia, I-25018 Montichiari, Italy; Assistance Publique-Hôpitaux de Paris et Université Paris-Sud 11 (P.C.), Department of Endocrinology and Reproductive Diseases, F-94275 Le Kremlin-Bicêtre, France; Neuroendocrine Unit (M.D.B.), Division of Endocrinology and Metabolism, University of Sao Paulo Medical School, 05311-970 Sao Paulo, Brazil; Neuroendocrine Unit (A.K.), Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114; Department of Internal Medicine (S.L.), Division of Endocrinology, Erasmus Medical Center, 3000 CA Rotterdam, The Netherlands; Division of Endocrinology CHUS (P.F.C.), Department of Medicine, Santiago de Compostela University, 15782 Santiago de Compostela, Spain; Department of Endocrinology (P.T.), Christie Hospital, Manchester M20 4BX, United Kingdom; Division of Endocrinology (E.G.), University of Turin, 10129 Turin, Italy; Pituitary Research Unit (K.H.), Garvan Institute of Medical Research, Sydney, New South Wales 2010, Australia; and Department of Medicine (S.M.), Cedars-Sinai Medical Center, Los Angeles, California 90048

Objective: The Acromegaly Consensus Group met in April 2009 to revisit the guidelines on criteria for cure as defined in 2000.

Participants: Participants included 74 neurosurgeons and endocrinologists with extensive experience of treating acromegaly.

Evidence/Consensus Process: Relevant assays, biochemical measures, clinical outcomes, and definition of disease control were discussed, based on the available published evidence, and the strength of consensus statements was rated.

Conclusions: Criteria to define active acromegaly and disease control were agreed, and several significant changes were made to the 2000 guidelines. Appropriate methods of measuring and achieving disease control were summarized. (*Clin Endocrinol Metab* 95: 3141–3148, 2010)
Information revolution
Influence of the Media and Internet...
Specialist Endocrine Nursing

• Patient education
• Dynamic testing
• Liaison with primary care
• Use of specialist therapies
• Nurse-led clinics
• National support network
• and much more...!