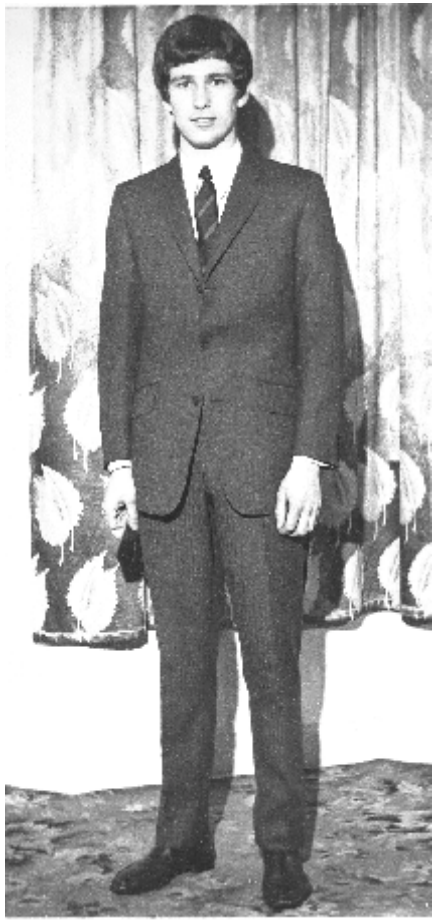
The present and future for newborn screening in Europe - A possible role for Eurogentest and ERNDIM (and of course an exciting opportunity for Brian to add to his wardrobe!

Dr Jim Bonham
Laboratory Director
Sheffield

Outline

- Metabolic EQA in 1991
- Why is screening different and maybe dangerous?
- An EU interest in rare diseases
- Current practice
- The benefits of screening
- The problems
- Where might we go in the future?
- A role for Eurogentest/ERNDIM

- A role for Brian, a man for all seasons



Metabolic EQA in 1991

- Little or no laboratory accreditation
- No international EQA schemes, some local and national schemes
- No attempt to identify or deal with poor performance
- No regular EU forum to discuss EQA

Why is screening different?

- The patients/families believe themselves to be well and this gives us a particular burden of responsibility
- The initial test does not in itself give a definitive answer. It simply separates those who are more likely to have the condition (and require follow-up) from those who are less likely to have it.

How can screening be defined?

- Screening is a public health service in which members of a defined population who do not necessarily perceive they are at risk of, or already affected by, a disease or complication are asked a question or offered a test, to identify those individuals who are more likely to be helped than harmed by further tests or treatments to reduce the risk of a disease or its complications.

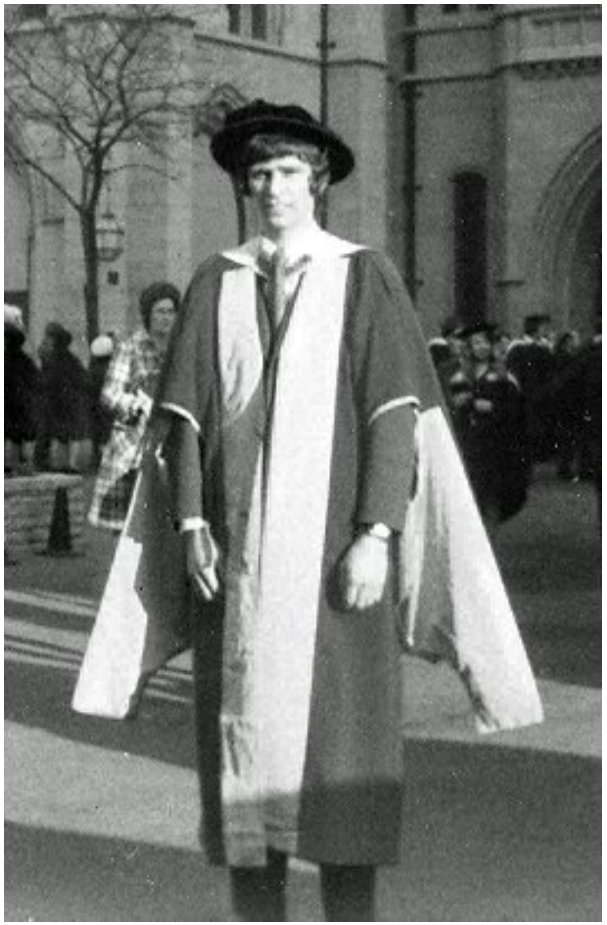
What kind of problems can arise?

The Neuroblastoma story

- Incidence of clinically detected disease 1:29,000
- When detected at <1y age at stage I,II or IVS the prognosis is much improved
- In 1985 it became possible to screen by measuring HVA and VMA in urine at 6 mo, taken up in Japan and Newcastle
- Survival in the screened population >90% compared with 50% in clinically detected cases
- However, after the introduction of screening the mortality rate due to neuroblastoma did not decline
- Two factors at work:
  - Poor sensitivity for cases that would go onto progress to clinically significant disease
  - Screening is differentially picking up the tumours that are least likely to progress and may spontaneously resolve.

An EU interest in rare diseases

- Defined as disorders with a prevelance of <1:2,000, rare disorders affect 1 in 17 people in the EU, that is 35 million
- In June 2009 the EU issued a Council Recommendation for an action in the field of rare diseases to cover:
  - Classification and coding
  - Establishment of European reference networks
  - Establishment of financial tools and governance systems
  - Community initiatives for definition of best practice for diagnosis and care including population screening
  - To deliver national plans by 2013
- A tender to look at screening practice
  - A report on the practices of NBS in the EU
  - An expert opinion document including a decision matrix on policies for development



So what are we doing in Europe?

Country	Screened infants	Number of labs	Country	Screened infants	Number of labs
Austria	83649	1	Latvia	21655	1
Belgium	121999	6	Lithuiania	34456	1
Bulgaria	74510	2	Luxembourg	6159	1
Cyprus	9749	1	Malta	4100	2
Czechia	118348	6	Netherlands	185743	5
Denmark	65000	1	Poland	421000	8
Estonia	15730	1	Portugal	99809	1
Finland	60794	18	Romania	226000	4
France	841931	22	Slovakia	56475	1
Germany	675000	11	Slovenia	20269	1
Greece	120852	1	Spain	498711	20
Hungary	95000	2	Sweden	110523	1
Ireland	74278	1	UK	797214	16
Italy	576000	40			

So what are we doing in Europe?

Country	Birth interval	Storage of spots (yrs)	Country	Birth interval	Storage of spots (yrs)
Austria	36-72h	10	Latvia	72-120h	7
Belgium	72-120h	5	Lithuiania	48-96h	25
Bulgaria	72-120h	20	Luxembourg	96-168h	8
Cyprus	96-168h	5	Malta	Cord blood	n/a
Czechia	48-96h	5	Netherlands	72-168h	5
Denmark	48-72h	1000	Poland	48-96h	1
Estonia	48-72h	100	Portugal	48-96h	12
Finland	Cord blood	n/a	Romania	48-96h	2-5
France	48-96h	1	Slovakia	72-96h	20
Germany	48-96h	0.25	Slovenia	72-120h	10
Greece	96-168h	3	Spain	48-96h	1-1000
Hungary	48-72h	1	Sweden	48-96h	1000
Ireland	72-120h	26	UK	797214	5
Italy	48-96h	1-10			

So what are we doing in Europe?

Country	MS/MS screen (exc PKU)	Country	MS/MS screen (exc PKU)
Austria	26	Latvia	0
Belgium	10	Lithuiania	0
Bulgaria	0	Luxembourg	0
Cyprus	0	Malta	0
Czechia	8	Netherlands	11
Denmark	11	Poland	0
Estonia	0	Portugal	23
Finland	0	Romania	0
France	0	Slovakia	0
Germany	8	Slovenia	0
Greece	0	Spain	20
Hungary	21	Sweden	0
Ireland	2	UK	1
Italy	26		

So what are we doing in Europe?

Disorder	Number screening	Disorder	Number screening
arg	5	scad	5
asa	5	vlcad	10
cit !	4	3-hmg	5
cit 2	3	3-mcc	5
hcy	7	ga 1	10
hptl-III	4	ga 2	5
msud	12	hcad	6
tyr 1	8	iva	9
tyr 2-3	4	mma	5
cud	5	mmabcl	5
cpt !	6	pa	7
cpt 2	7	bkt	4
lchad	9		
mcadd	11		

So what are we doing in Europe?

Country	Lab accreditation	EQA	Country	Lab accreditation	EQA
Austria	ISO9001	No data	Latvia	None	CDC
Belgium	ISO 15189	RIVM	Lithuiania	None	No data
Bulgaria	Nat standard	Japan interlab	Luxembourg	None	No data
Cyprus	None	No data	Malta	None	No data
Czechia	ISO 15189/9001	No data	Netherlands	ISO 15189	CDC,DGKC, NEQAS
Denmark	ISO17025	CDC	Poland	Nat standard	CDC, NEQAS
Estonia	ISO9001	CDC	Portugal	None	No data
Finland	ISO15189	No data	Romania	None	No data
France	None	AFSSAPS	Slovakia	None	CDC
Germany	ISO 15189	CDC	Slovenia	None	NEQAS
Greece	None	CDC	Spain	ISO 15189	No data
Hungary	ISO 9001	CDC	Sweden	ISO 15189	CDC
Ireland	ISO 15189	No data	UK	ISO 15189	NEQAS
Italy	ISO 9001	CDC			

The benefits of screening

- Reduces anxiety and uncertainty for families
- Permits genetic counselling
- Removes inequality
- Cost effective
- Improves outcome

The benefits of screening

- Ann Neurol 2010, Herringer J et al
  - 52 GA1 patients detected by screening 1999- 2009
  - 37 treated on advised guideline, 35 asymptomatic, mild dystonia
  - 9 without low lysine or carnitine, 5 asymptomatic
  - 6 without emergency regimine, 0 asymptomatic

The problems

- Little standardisation of laboratory practice, accreditation or EQA
- Few recognised guidelines and patchily applied
- Treatment by non specialist centres
- Lack of agreed policies to handle screen positive results, patient experience varies
- Good outcome studies are rare and there is no agreement about case definitions that would permit proper study

What can ERNDIM and Eurogentest offer?

- Newborn screening conducts around 40 million tests per year in the EU and is by far the biggest provider of "genetic" testing
- It is likely that this will rise to 65 million by 2015
- It needs to be centre stage in Eurogentest
- Screeners may know little about metabolic disease are frequently not accredited and use a variety of largely non-EU EQA providers without any poor performers policy
- Eurogentest needs to be involved in describing best practice
- ERNDIM needs to be involved in education and supplying EQA
- Brian needs to be our man at the EU, he does not need to retire but rather be re-cycled