

**Disclaimer:** These notes were taken by Ruth Dameron at the LMBBS Conference in Houston, June 17, 2006. There has been no attempt to verify accuracy. Do not quote the speakers based on these notes!

### **Session 1 -- History – Richard Lewis**

#### **Morning and half of afternoon program:**

Nutrition – Kay Motil  
 Syndrome X – Balasubramanyam  
 Kidney – Eileen Brewer  
 Speech – Alice Brackett  
 Surgery - xx  
 Genetics – Nico Katsanis  
 Treatment? – Richard Lewis  
 Ask the Doctors

Through the combination of these sessions, we hope to learn:

Where have we been?  
 How did we get here?  
 Where are we now?  
 Where are we going”

### **Overview of BBS**

Who were Laurence, Moon, Bardet, and Biedl?

1450 BC relief – blind harpist

400 AD Inca carving – blind flutist

41 million blind in the world

3 million blind in the U.S.

More than 25% of childhood blindness is genetic

Dr. Jim Lupsky and Dr. Katsanis are researchers.

Dr. Lewis is clinician.

The Eye

3 embryonic layers

Sites for genetic disease

25% of all human genetic disorders involve the eye (RHD: I'm not sure I got that right)

Gene --> RNA--> Protein--> substrate --> clinical disease

Dr. Lewis sees the disease

Over the last 25 years (Lewis came to Baylor in 79) retinal disease genes have been identified and mapped with increasing frequencies

**Dystrophy** – dys – bad, unlucky, negative  
 trophy – nourishment nurture

Dystrophy: A primary bilateral symmetric genetic disorder with distinct histopathologic and clinicopathologic features

Eye dystrophy: A primary process intrinsic to metabolism of eyes, affects both, and necessarily is gene based. Distinctive features when we look at patient clinic and when we look at the cells under the microscope. Starts out in normal cells; does not involve blood vessel abnormalities.

**Degeneration** – deterioration from higher level to lower level, extrinsically affects tissue. Not genetic, not symmetric necessarily. Extrinsic: age, trauma, inflammation.

People first thought the retina problem was the result of an infection so it was called *retinitis*.

Retinitis pigmentosa – there are 50+ forms – look like each other in the eye.

In 1985, looked to see what RP was associated *with*. “Syndrome” comes from syn-with and drome-racecourse. So a syndrome is a concurrence of several signs in a disorder that appear together but don’t need to seem to be related on the face of it. For example Usher’s Syndrome involves blindness and deafness.

In 1985, we thought “if we could find families with syndromes, then could we work backwards to find the genes associated with the RP that the syndrome includes?” And that’s where this story begins for Dr. Lewis.

BBS’s retina features are not really RP but look similar.

- **R. Liebreich** – 1865(?); night blindness, normal parents, retarded, 6 toes on each foot and hand.
- **Laurence**, John – English – 1866 wrote the first major handbook of ophth surgery. Founded the Ophth Review. One of his resident students was Robert Moon, born in 1845 in England, on staff at same hospital. 1879 moved to Philadelphia, Jefferson College. Practiced in Phila until 1912; died in 1914. Laurence and Moon in London wrote up 4 cases of rp in the same family accompanied by a general imperfection of development in 1866. 1 girl and 3 boys out of 7 siblings, short, ataxia, mentally dull, infantile external genitalia.
- **Alfred Gordon** – 1907 – Cases allied to amaurotic family idiocy with remarks on the pathogenesis of the affection. Russian Hebrews, mental deficiency, blindness early in life, small genitalia. Also polydactyly. Childish behavior even when adolescent. Sister was large, adipose, mentally slow, and apathetic, articulation was not distinct, intonation was nasal, blindness at 3 yrs., apathetic personality. Thought it was Tay-Sachs Disease.
- **Georges Bardet** – med student in Paris – had to produce a thesis to finish medical school. He described congenital obesity, polydactyly, opoor vision, slow learner.
- **Arthur Biedl** – 1869 – Hungary – wrote the first classic textbook of endocrinology in Europe. His interest had to do with the obesity which he thot was caused by alterations in the pituitary gland.
- The tradition has been to name things in medicine after the people who first described it.
- Laurence & Moon talk of lower limb weakness, don’t mention polydactyly; if they saw it, it’s hard to imagine they would not mention it.

**Defining features of BBS now:**

- extra fingers and toes
- weight gain at end of 1st year of life
- retinal dystrophy
- hypogonadism
- renal
- learning difficulties

BBS is the second most commonly missed diagnosis of RP by ophth. (The first most missed is Usher’s because they miss the deafness).

Average age of LMBBS in his data – 7.5 years.

Why do all the features occur and what clues can we use to explain other things –  
Can this syndrome help find causes for RP, retardation, obesity, speech pathology?