

GEORGE WILLIAMS

Medical Matters in CHARGE



Charge Syndrome Medical Management

George Williams

Thank you Tim Hartshorne
for some of the slides the slides

DIAGNOSIS

- Mitchell* – AI/GEN and Diagnostic model, J Med Syst 9, 425-436, 1985
- Pagon* - J Paed, 99, 16, 122-128, 1981
- Blake* - Clin Paed, 37, 159-173, 1998
- Verloes* – Adding 3C: **C**oloboma, **C**hoanal atresia & abnormal ssCs, Eur T Hum Gen, 15, 389-399, 2007

Differential Diagnosis

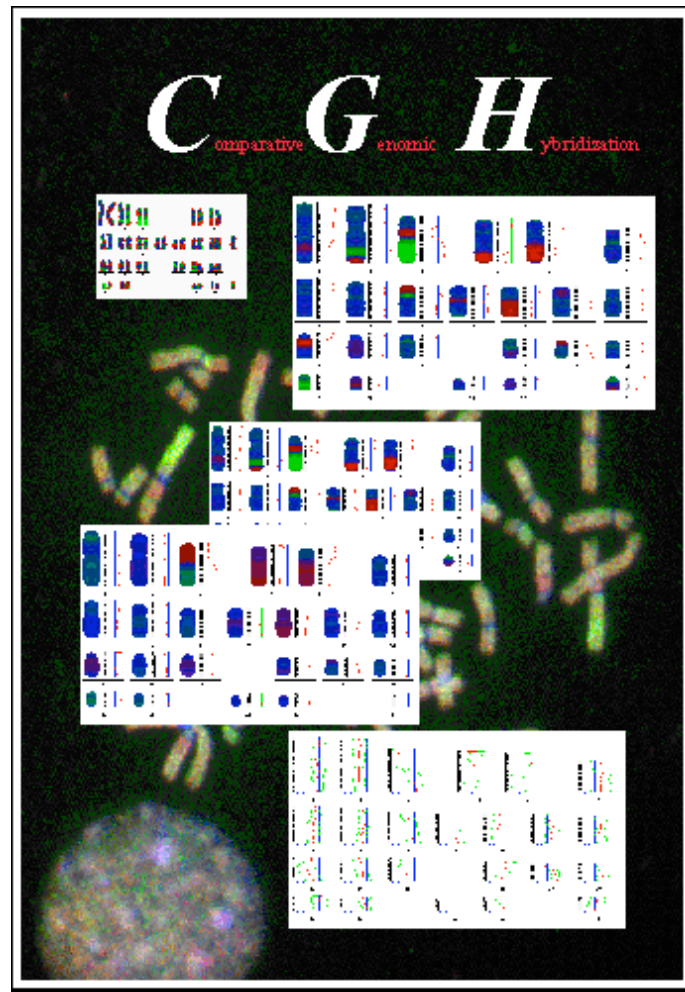
- VCFS and DiGeorge syndromes – 22q11.2
- Vacterl association
- Kabuki syndrome
- Pax2 mutation
- Cat-eye syndrome
- Joubert syndrome
- OAVS
- Retinoic embryopathy



The Power of Array CGH:
The identification of an important gene,
CHD7 involved in CHARGE syndrome

Conny van Ravenswaaij,
Lisenka Vissers, Ronald Admiraal,
Jane Hurst, Bert de Vries, Erik Schoenmakers,
Han Brunner, Joris Veltman, Ad Geurts van Kessel

Comparative Genomic Hybridization



Syndrome and not Association

CHD 7 mutations

- CHD 7 in 2/3 affected individuals
- Long arm chromosome 8 (8q12)
- 1/10,000 births
- AD disorder
- Dysblastogenic and dysneurulative process
- CHD7 is DNA regulator
- Nonsense(45%), frame shift (25%), splice site (19%), missense (12%) and intragenic deletion (0.5%)
- Genotype – phenotype correlations not done yet

Issues

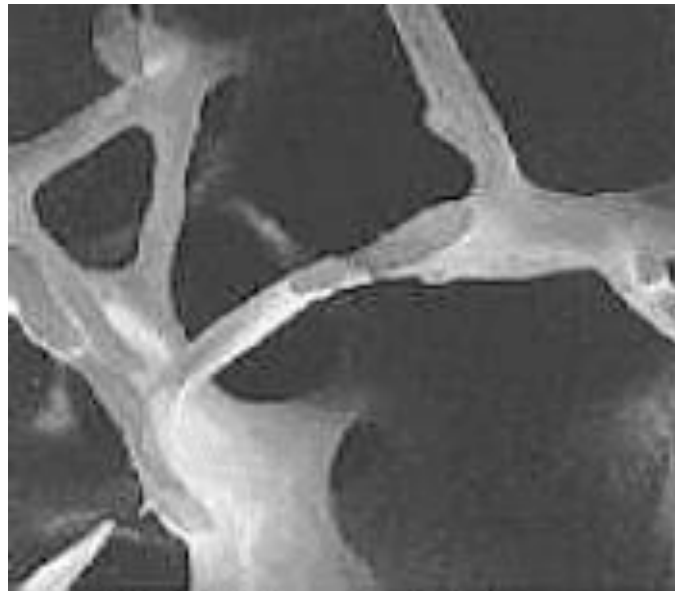
- Suck-swallow-breath
- GORD
- Infection
- Cardiac disease
- TOF
- Choanal atresia
- Tracheostomy
- IV nutrition

Issues

- Stress and pain
- Sensory bombardment and intrusive enviro
- Multiple procedures, surgery and anaesthetics
- Communication
- Tapping into the senses
- Support and networking
- Medical monsters
- Preparation for home
- Extreme challenging behaviour

Bone Health

- Recent study by Blake, 9 of 10 individuals with CHARGE had low bone mineral density



Bone Health is Based On

- Genetic predisposition
- Sex hormone levels in adolescence
- Physical activity
- Nutrition
 - Calcium
 - Vitamin D
- Fractures in early childhood

Osteoporosis reference

Risk factors for poor bone health in adolescents
and adults with CHARGE syndrome

Kim D Blake et al, Am J Med Gen (2007)
Part A, 143A, 839-845

Charge Medical References

- www.emedicine.com/PED/topic367.htm
- European J of Hum Gen (2007) 15, 389-399, Charge syndrome – an update Sanlaville and Verloes (free from Orphanet)
- http://en.wikipedia.org/wiki/CHARGE_syndrome
- <http://www.mhaspectofdd.com/abstracts/Vol7Num2/1.htm>

Genetic sources

- www.agsa-geneticsupport.org.au
- www.genetics.com.au
- www.geneticalliance.org
- www.kumc.edu/gen/support
- <http://gslc.genetics.utah.edu/>
- <http://ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=charge>
- <http://www.nature.com/ng/journal/v36/n9/abs/ng1407.html>
- OMIM – Charge Syndrome and CHD 7

Charge websites

- <http://www.austcharge.com.au>
- <http://www.chargesyndrome.ca/>
- <http://www.chargesyndrome.org/>
- <http://www.charge-syndrom.de/>
- <http://www.chargesyndrome.info/>
- <http://www.sense.org.uk/>
- <http://www.cdbra.ca/>
- <http://www.dblink.org/lib/topics/charge-med.htm>
- http://www.familyvillage.wisc.edu/lib_chgs.htm

Hypogonadotrophic hypogonadism-HH

- Charge syndrome includes HH and abnormal olfactory bulb development – Netchine I et al, J Clin Endo & Met, July 18, 2005
- Endocrine and radiological studies in patients molecularly confirmed Charge syndrome – Asakura Y et al, JCEM, 2008, 93 (3) 920-924
- Olfactory abnormalities in Charge syndrome: imaging findings of a potential major diagnostic criterion – Blustajn C et al, AJNR, 2008, 29 (7) 1266-1269

Quote from J S Molloy - 1963

As each star differs in brightness, so do the children of man,

Yet each serves its purposes in one nation under God

and each is entitled to an opportunity to achieve his full potential

and to adjust to his environment to grow physically, emotionally, intellectually, socially and spiritually