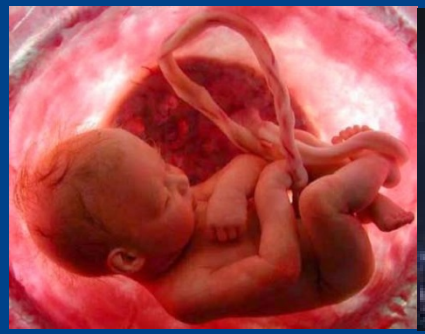
Maastricht UMC+

Rare Disease Day 2019

Maastricht, february 2019

Connie Stumpel



Diagnosis unknown!

- Example from real life

- Some general thoughts

- Take home messages

Girl born in 1981

- Second child
- Cleft palate
- Fallot tetralogy
- Scoliosis
- Dysmorfism

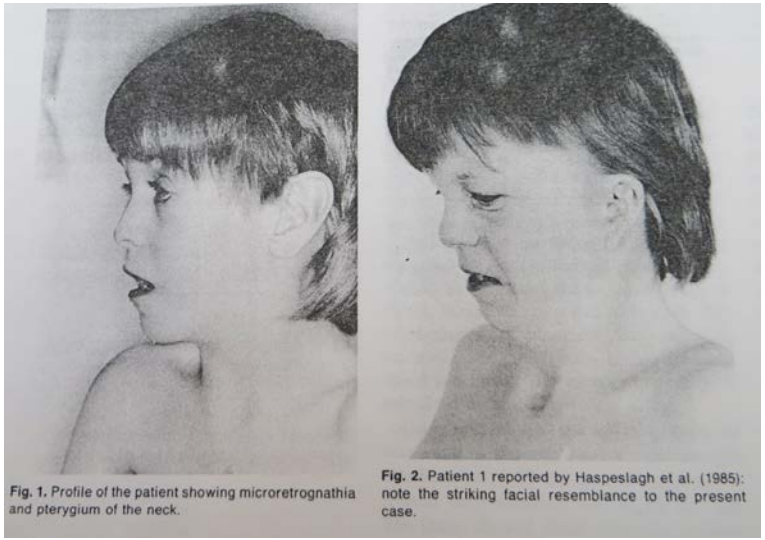
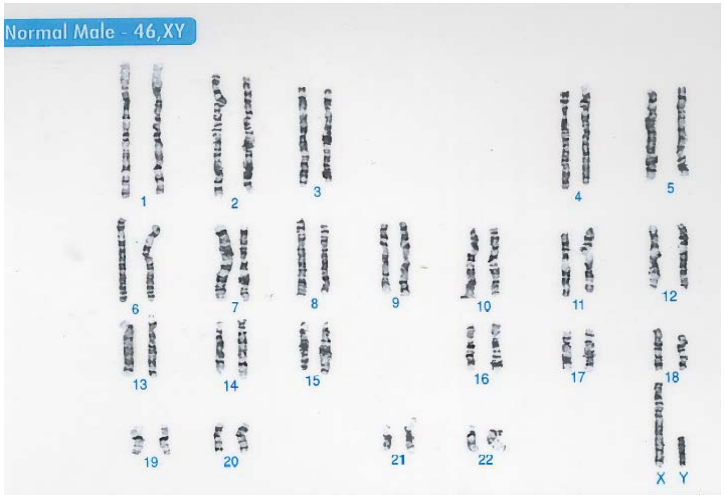


Fig. 1. *Profile of the patient showing microretrognathia and pterygium of the neck.*

Fig. 2. Patient 1 reported by Haspeslagh et al. (1985): note the striking facial resemblance to the present case.

- Clinical diagnosis of Haspeslagh syndrome

Chromosomes, FISH study, all normal over the years



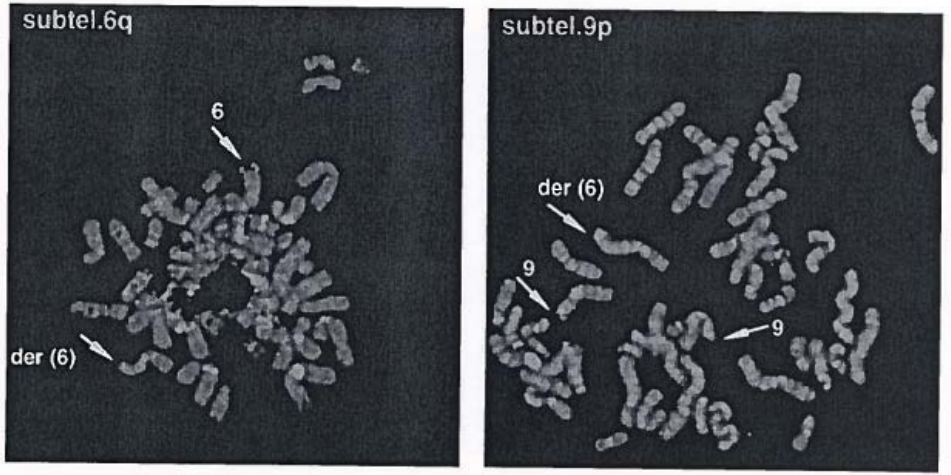
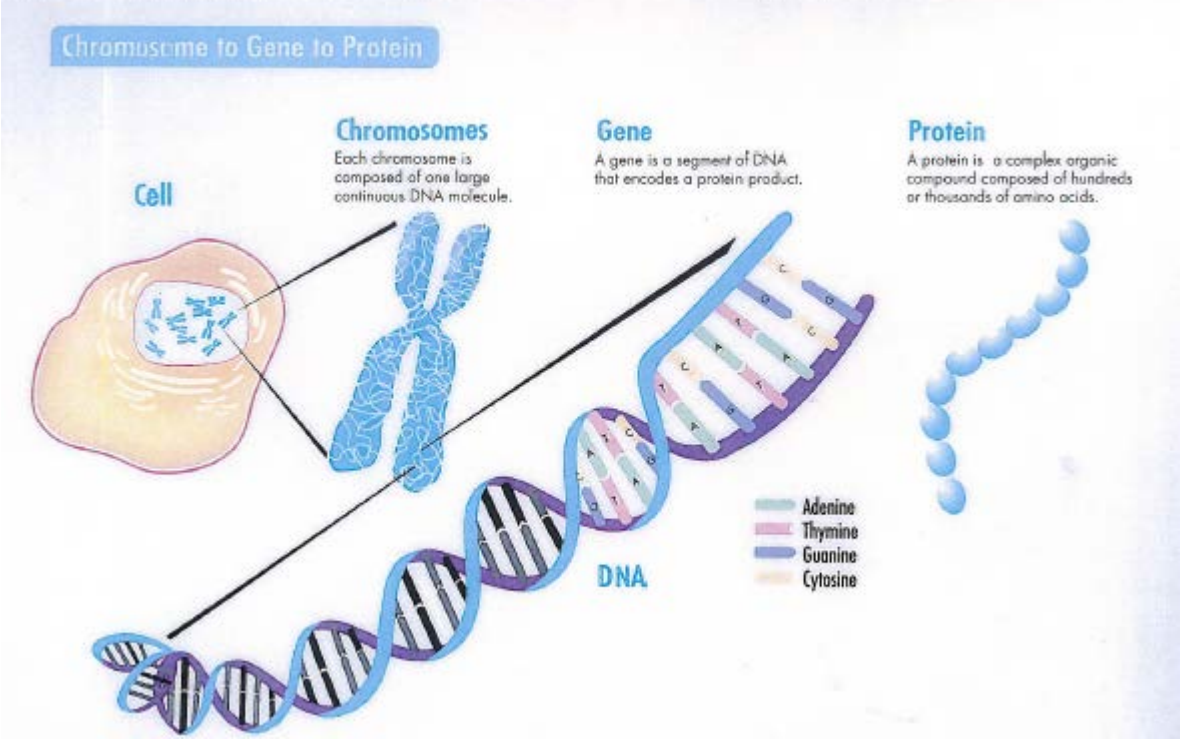
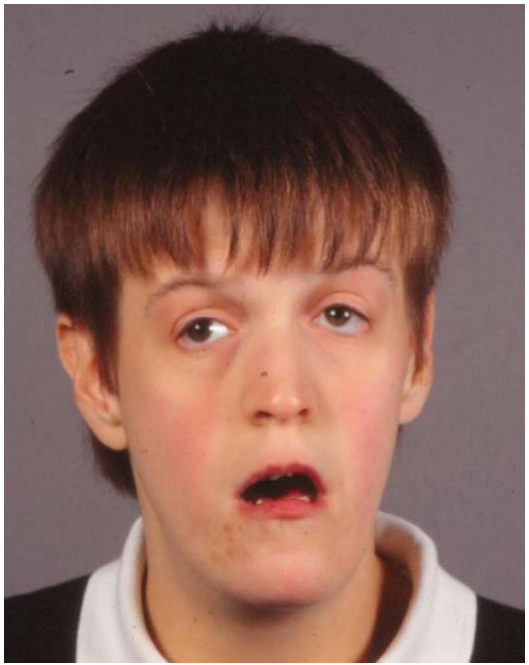


Fig. 1. FISH using subtelomeric probes for chromosomes 6q left panel and 9p (right panel), showing unbalanced translocation with partial monosomy 6q and trisomy 9p in one of the patients.

Follow up because of marriage of her sister



34 years of age: moderate/severe ID



Exome sequencing:

DDX3X; ChrX(GRCh37)

g.41204440G>T; NM_001356.4
c.1033G>T (p.(Val345Leu))
heterozygoot/ DE NOVO

Am J Hum Genet. 2015 Aug 6; 97(2): 343–352.
doi: 10.1016/j.ajhg.2015.07.004
PMCID: PMC4573244

Mutations in *DDX3X* Are a Common Cause of Unexplained Intellectual Disability with Gender-Specific Effects on Wnt Signaling

Lot Snijders Blok,[1,48] Erik Madsen,[2,48] Jane Juusola,[3,48] Christian Gilissen,[1] Diana Baralle,[4] Margot R.F. Reijnders,[1] Hanka Venselaar,[5] Céline Helsmoortel,[6] Megan T. Cho,[3] Alexander Hoischen,[1] Lisenka E.L.M. Vissers,[1] Tom S. Koemans,[1] Willemijn Wissink-Lindhout,[1] Evan E. Eichler,[7,8] Corrado Romano,[9] Hilde Van Esch,[10] Connie Stumpel,[11] Maaike Vreeburg,[11] Eric Smeets,[11] Karin Oberndorff,[12] Bregje W.M. van Bon,[1,13] Marie Shaw,[13] Jozef Gecz,[13] Eric Haan,[13,14] Melanie Bienek,[15] Corinna Jensen,[15] Bart L. Loeys,[6] Anke Van Dijck,[6] A. Micheil Innes,[16] Hilary Racher,[16] Sascha Vermeer,[17] Nataliya Di Donato,[18] Andreas Rump,[18] Katrina Tatton-Brown,[19] Michael J. Parker,[20] Alex Henderson,[21] Sally A. Lynch,[22] Alan Fryer,[23] Alison Ross,[24] Pradeep Vasudevan,[25] Usha Kini,[26] Ruth Newbury-Ecob,[27] Kate Chandler,[28] Alison Male,[29] the DDD Study, Sybe Dijkstra,[30] Jolanda Schieving,[31] Jacques Giltay,[32] Koen L.I. van Gassen,[32] Janneke Schuurs-Hoeijmakers,[1] Perciliz L. Tan,[2] Igor Pediaditakis,[2] Stefan A. Haas,[33] Kyle Retterer,[3] Patrick Reed,[3] Kristin G. Monaghan,[3] Eden Haverfield,[3] Marvin Natowicz,[34] Angela Myers,[35] Michael C. Kruer,[35,36] Quinn Stein,[36] Kevin A. Strauss,[37] Karlla W. Brigatti,[37] Katherine Keating,[38] Barbara K. Burton,[38] Katherine H. Kim,[38] Joel Charrow,[38] Jennifer Norman,[39] Audrey Foster-Barber,[40] Antonie D. Kline,[41] Amy Kimball,[41] Elaine Zackai,[42] Margaret Harr,[42] Joyce Fox,[43] Julie McLaughlin,[43] Kristin Lindstrom,[44] Katrina M. Haude,[45] Kees van Roozendaal,[11] Han Brunner,[1,11] Wendy K. Chung,[46] R. Frank Kooy,[6] Rolph Pfundt,[1] Vera Kalscheuer,[15] Sarju G. Mehta,[47,49] Nicholas Katsanis,[2,49,*] and Tjitske Kleefstra[1,49,**]

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- Cleft palate 3/38
- Scoliosis 4/38
- ID mild to severe

- Not recognizable!

Do we need to solve the unsolved rare diseases?

YES!

Perspective from patiënts

Perspective from professionals

Better care with a correct diagnosis

Genetic counseling needs a correct diagnosis

Influencing factors in finding a rare disease

A child with congenital anomalies/developmental delay is under medical care

Adults may be lost from medical care; the role of the GP is more pronounced

With or without intellectual disability matters

Molecular technology eg exome sequencing

Increasingly effective in solving rare diseases eg those with an intellectual disability and/or neurological disease.

For specific diseases the gene may be known.

For medical issues eg immunologic diseases gene panels exist.
The yeald varies.

Not everything is genetic! 80% of the rare disease is!

How to deal with our goal to solve the unsolved?

- Awareness is a continous issue
- Teaching: students, collegues

- Creating platforms for patiënts and professionals
- VSOP with platform ZON, Witte Raven, UMC's, EMRaDi, ERN's

- How to avoid confounding physical complaints to be mistaken for rare diseases?

There is so much expertise

Recognized expertise centers in the Netherlands, Belgium and Germany

ERN’s have databases to discuss unknown patients

Where is the gap?

Is it awareness?

Is it knowlegde?

Is it the drive to solve the unsolved?

Is it the patience/acceptance of not knowing?

Take home messages

- Be aware and curious
- Do not give up

- Learn from each other

- Care, Share and Cure is the ERN motto!