From pediatric history. Important personalities in relation to some genetic defects – “trisomies”

Ingrid Brucknerová 1, Anna Holomáňová 2, Mojmír Mach 3, Eduard Ujházy 3

1 1st Department of Pediatrics, Medical Faculty, Comenius University, Bratislava, Slovakia
2 Department of Anatomy, Medical Faculty, Comenius University, Bratislava, Slovakia
3 Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Bratislava, Slovakia

Correspondence to: Assoc. Prof. Ingrid Brucknerová, MD., PhD.
1st Department of Pediatrics, Medical Faculty, Comenius University,
Limbova 1, 833 40 Bratislava, Slovakia.
tel: +421-259 371 209; e-mail: osmium@centrum.sk

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INTRODUCTION

The development of the fetus depends on many factors. The optimal physiological growth of the fetus requires a good genetic predisposition, healthy parents, not only the mother, and healthy surroundings. The development of the fetus is sometimes changed by spontaneous mutation, infection or by unknown mechanisms.

Some visible anomalies can be confirmed during prenatal development thanks to prenatal screening methods. A large group of diseases can be confirmed after delivery (metabolic disorders, infections, etc.) (Embleton et al. 1996; Kovács et al. 2010; Šustrova et al. 2004).

The consequence of a pathological impulse can be the development of a malformation (a primary defect of structure, which arises from a localized disorder in morphogenesis) or a deformation (an alteration in structure or in the shape of a certain part that has differentiated normally). Changes in the number of chromosomes belong to the group of chromosomal anomalies with the highest occurrence rate. The most frequent anomalies are trisomy 13, 18 and 21.

The risk of trisomy is enhanced not only with the increasing maternal but also with the rising paternal age.

IMPORTANT PERSONALITIES IN MEDICINE

Klaus Patau (1908–1975)

He was born in 1908 and studied in Germany (Figure 1). During the years 1938 and 1939, he worked in London. From 1939 to 1947 he worked at the Kaiser Wilhelm Institute for Biology in Berlin. An important year in his life was the year 1948, when he emigrated to the United States, where he later obtained the American citizenship. He devoted his interest to the genetic material of the human body. In 1960 he first reported on the...
presence of an extra chromosome in trisomy 13. He worked together with his wife in the Department of Genetics at the University of Wisconsin-Madison.

The name of this famous geneticist is joined with trisomy 13, although the first description of this anomaly appeared in 1656 by Thomas Bartholin.


Born on March 26, 1928 in London, Edwards (Figure 2) was an English physician and medical geneticist. He studied at Cambridge University (1949–1952) and from 1954 to 1956 at the University of Birmingham. He achieved the membership of the Royal College of Physicians (1956), Fellowship in 1979, and became Fellow of the Royal Society in 1979.

His main interest was genetics. He is the author of the description of trisomy 18, the so-called Edwards's syndrome or trisomy E, which he discovered in 1960. He worked in Oxford, Philadelphia, and Birmingham. As Visiting Professor of Pediatrics he was working in New York and was a Staff Member of the New York Blood Center. The year 1971 was an important year in his life as he became professor of human genetics at the University of Birmingham. He died on October 11, 2007 (McKusick 2007).

All his work was focused on comparative gene mapping, on analysis of human genetic linkage and the identification of X-linked hydrocephalus.

**John Langdon Haydon Down (1828–1896)**

Down was born on November 18, 1828 in Torpoint in Cornwall (Figure 3). In his childhood he was interested in mathematics. His career began in London where he at the age of 18 years started to work for a surgeon in Whitechapel Road, where he had to extract teeth and to do services like washing bottles and dispensing drugs. Later he entered the pharmaceutical laboratory in Bloomsbury Square. He won a prize for organic chemistry. He died on October 7, 1896.

He is best known for his description of a relatively common genetic disorder that is now called Down syndrome.

**CHARACTERISTICS OF TRISOMIES 13, 18 AND 21**

Trisomy 13, Patau's syndrome, is the least common and most severe of the viable autosomal trisomies. In most cases, the affected child dies within the first month; only 10 % survive beyond the first year.

Trisomy 18, Edwards's syndrome, results from no disjunction during the first or during the second meiotic stage. The extra chromosome 18 is in 90–97 % of maternal origin (Embleton et al. 1996).

Trisomy 21, Down's syndrome is characterized by the presence of supernumerary chromosome 21, known as trisomy 21. It is a common chromosomal aberration in humans. It occurs in three forms: free trisomy, translocation or mosaic trisomy (Šustrova et al. 2004).

The risk factors for the disease are not fully known. The following situations have been implicated in its occurrence: a higher age of the mother, environmental factors – radiation and additive substances – tobacco, alcohol, drugs, etc. increase the likelihood of occurrence of Down's syndrome (Kovács et al. 2010).

In the clinical picture, in most cases the newborn presents the typical somatic signs at birth (Table 1), though the presence of individual signs may differ.
Trisomies

DISCUSSION

We present three very important geneticists from the history of previous centuries, Patau, Edwards and Down, who confirmed the most frequent chromosomal abnormalities. Even nowadays, the contribution of all three physicians presented has an impact on the clinical work of pediatricians caring for children with dysmorphic features.

The clinical presentation of the anomaly of the number of chromosomes in trisomy 13, 18 and 21 is somewhat different. During physical investigation, it is very useful to know the most prominent features (Table 1). There are also slight differences in the form of congenital changes of organs, which require detailed knowledge of anatomy and embryonic development (Holomáňová & Brucknerová 2000; 2001; 2002; 2003). In all forms of the described trisomies, there is an increased frequency of prenatal and perinatal asphyxia and the prognosis is not very optimistic.

On establishing the differential diagnosis, we have to think also about congenital infection. Congenital infection can be assumed when the following manifestations are found on physical examination: microcephaly/macrogencephaly, low birth weight, growth retardation, stigmatisation, dysmorphology, enlargement of the liver and spleen, hearing loss, congenital anomaly of organs. The final diagnosis is confirmed by serologic investigations. An unknown metabolic disease can present with dysmorphic features, severe convulsions, enlargement of the liver and spleen, hypoglycemia, anemia, metabolic acidosis, etc.

The care of a child with genetic abnormality must be multidisciplinary, involving genetic counseling, assessment by a general practitioner for children, by a surgeon, cardiologist, neurologist, speech therapist, special educator, audiologist, ophthalmologist, otorhinolaryngologist, immunologist, physiotherapist and orthopedist. It requires also the awareness of both parents.

CONCLUSION

The physiological course of the development of the fetus can be changed due to infection and anomalies in the shape and number of chromosomes. Also genetic predisposition to some diseases can play an important role.
role. Mostly the actual reason is unknown. The probability of the occurrence of prenatal and perinatal neonatal asphyxia is very high.

We present only three very important names of physicians who by their enthusiastic and seminal accomplishments contributed considerably to the realm of knowledge in pediatrics. We pay tribute to their achievements.

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