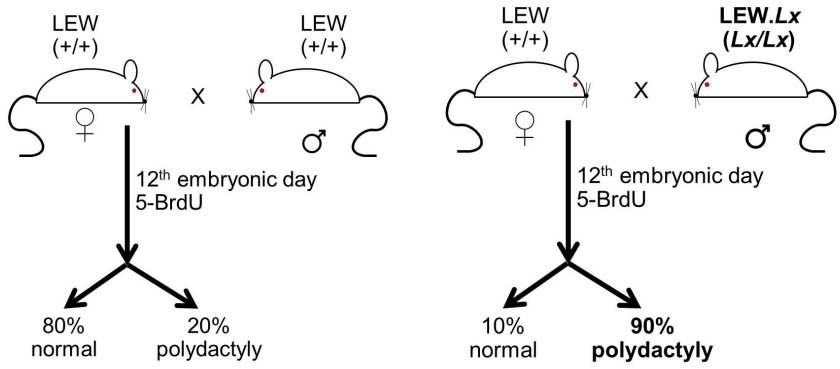
Introduction: Congenital anomalies (also birth defects or congenital malformations) are morphological defects resulting from an abnormal prenatal development. We may observe them either in the newborns ("congenital" anomalies) or today even during ultrasound examinations during the pregnancy ("fetal" anomalies). Morphologic defects may be part of syndromes caused by chromosomal aberrations (Down syndrome), monogenic syndromes (Marfan syndrome), but they often have multifactorial etiology or they are result of prenatal exposition to selected adverse factors. Those factors are known as **teratogens**.

According to their etiology and multiplicity we may classify those anomalies as follows:

- **Malformation** is caused by an abnormal development of an organ / tissue that is abnormal from the beginning.
- **Disruption** is caused by destructive process affecting an organ / tissue, which initially developed normally.
- **Deformation** is caused by an abnormal physical force that damages a healthy organ / tissue.
- **Dysplasia** is caused by an abnormal organization of the cells in the organ / tissue.
- **Isolated anomaly:** an anomaly that is not associated with any other condition (e.g. isolated polydactyly).
- **Sequence:** multiple anomalies that result from the pathologic cascade caused by a primary insult (e.g. Potter's sequence).
- **Association:** selected congenital anomalies that tend to develop all together – in an association (e.g. VATER association).
- **Syndrome:** complex of phenotypic traits (anomalies) that are typical for a defined clinical diagnosis (e.g. Down syndrome).

Task 1 (in the book - task 2, page 171 (164))



What phenotype do you expect in offspring of the drug-induced polydactylous rats?

……

How do we call this result of drug action (induced phenotype that resembles genetic disease)?

……

Task 2 (in the book - task 3, page 172 (164))

Worked out by: …… Group:…… Checked by:……

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If polydactyly is a recessive trait in the laboratory rat (genotype of recessive homozygotes is Lx/Lx), what incidence (in %) of polydactyly will you expect among offspring of heterozygote (+/Lx) rats that were exposed to the effect of 5BrdU during their prenatal development? Consider following situations:

a) Both parents are normodactylic:
b) Both parents are polydactylic:
c) One parent is normodactylic, one parent is polydactylic

a) **b)** **c)**

Task 3 Clinical syndromology (task not in the book)

In the clinical practice we often encounter phenotypes that may be explained by various clinical syndromes with different etiology (including genetic and non-genetic causes). Evaluate the phenotype of four different 16-year girls who were referred for clinical genetic examination because of primary amenorrhea. Using the results of selected laboratory examinations – propose the most probable diagnose (syndrome) for each of the girls and estimate their prognosis regarding future reproduction.

Trait	Girl 1	Girl 2	Girl 3	Girl 4
Relative height	<1. percentile	90th percentile	70th percentile	50th percentile
Menarche	0	0	0	0
Brest development	delayed	normal	delayed	normal
Pubic hair	normal	missing	normal	normal
Vagina	normal	blind ending	normal	extremely narrow and blind ending
Uterus	+	-	+	-
Fallopian tubes	+	-	+	-
Gonads	streak gonads	Dysgenetic testes in small pelvis	streak gonads	normal ovaries, normal location
Psychomotor development	normal	normal	normal	normal
Craniofacial dysmorphia	mild	-	-	-
Karyotype	45,X	46,XY	46,XY	46,XX
SRY locus (FISH)	not present	present	not present	not present
Resistance to androgens	-	+	-	-
Diagnosis				
Prognosis regarding future reproduction				