Sex and Gender Differences

BIRTH DEFECTS

Congenital anomalies, any physical and/or mental impairment/dysfunction/alteration that occurs during embryonic/fetal development

	FEMALE	ALL	MALE

Risk Factors	• Congenital heart disease
	  ◦ Atrioventricular septal defects in Down Syndrome
	• Protective factor:
	  ◦ **Higher catecholamine levels** provide **support during hypoxia** at preterm delivery, therefore resulting in **less oxidative stress**
		Specific risk factors vary by type of defect
		• Before conception:
		  ◦ Parental genetics
		  ◦ Consanguinity
		  ◦ Infertility problems
		  ◦ **A**ssisted **r**eproductive **t**echnologies (**ART**s)
		  ▪ Septal heart defects, cleft lip, neural tube defects, tetralogy of Fallot, etc
		  ◦ **Advanced maternal age (over 35):** numerical chromosomal disorders (e.g. trisomy 21)
		  ◦ **Advanced paternal age (over 40):** spontaneous congenital disorders and neuropsychiatric conditions (e.g. schizophrenia and autism)
		• Pregnancy:
		  ◦ maternal substance use, folic acid deficiency, obesity, uncontrolled pre-gestational diabetes, phenylketonuria, teratogenic drug use, infections, exposures (ionizing radiation, organic mercurials, and lead)
			• Male fetuses at **higher risk** secondary to maternal smoking
			• Pulmonary and cardiac disorders (i.e. Tetralogy of Fallot)
			  ◦ Preterm males at higher risk due to **delayed** lung maturation

Prevalence	• **Higher rate** of
	  ◦ neural tube defects (e.g. anencephaly)
	  ◦ endocrine system defects (e.g. congenital hypothyroidism)
	  ◦ choledochal cyst
	  ◦ congenital hip dysplasia
	  ◦ Trisomy 18
	  ◦ atrial septal defect
	  ◦ patent ductus arteriosus
		• 1 in 33 babies is born in the US with birth defects
		  ◦ ~110,000 annually
		  ◦ 50% of first-trimester miscarriages have chromosomal anomalies
		• Commonly: clubfoot, cleft palate, limb deformities, pulmonic stenosis/atresia, and Down Syndrome
			• **Higher rate** of
			  ◦ omphaloceles
			  ◦ pyloric stenosis
			  ◦ clubfoot
			  ◦ cleft palate
			  ◦ sex organ defects
			  ◦ urinary tract defects
			  ◦ ventricular septal defect
			  ◦ pulmonic stenosis and atresia

Presentation

Examples of the most common birth defects

- Clubfoot: inverted foot turned sideways or pointing up
- Cleft palate: split in the roof of the mouth and/or upper lip
- Pulmonic stenosis/atresia: heart murmurs, chest pain, shortness of breath, fatigue, fainting, and blue-tinted skin
- Down Syndrome:
  - many have distinctive physical features such as a smaller head, flat face, poor muscle tone, and short height
  - varying levels of cognitive impairment and health issues such as heart defects

Pathophysiology	• **Less** commonly in females
	• Phenotypically **less** severe
	  ◦ Unless homozygous for the deleterious allele
		• May result from: genetic, infectious, nutritional, or environmental factors
		  ◦ Often difficult to identify exact causes
		• Sex differences arise when the defect is X-linked
		  ◦ In heterozygous females, the allele is not expressed in all cells
		  ◦ In males, the allele is expressed in all cells
			• **More** commonly affected by X-linked variants
			  ◦ Due to single X chromosome

Screening

- Available screening tests include: ultrasound, blood and urine tests, amniocentesis, genetic testing, CT, MRI, and CNS scans, echocardiograms, fundoscopy, and more
- Non-invasive prenatal testing (NIPT): analyzing fetal DNA in the maternal blood (AFP, hCG, estriol, inhibin)

Treatment

- Primary prevention measures: addressing modifiable risk factors
- Treatments to help reduce symptoms and support patient goals
  - Dependent on symptoms, age, general health, and severity
  - Includes: surgery, medication, physical or occupational therapy, education intervention
- Ensure regular healthcare and follow-up
  - Multidisciplinary team can include counselors, social workers, genetic counselors, PTs, speech therapists, dietitians

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SEX and GENDER HEALTH COLLABORATIVE of the American Medical Women's Association

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Definitions & Disclaimers

References