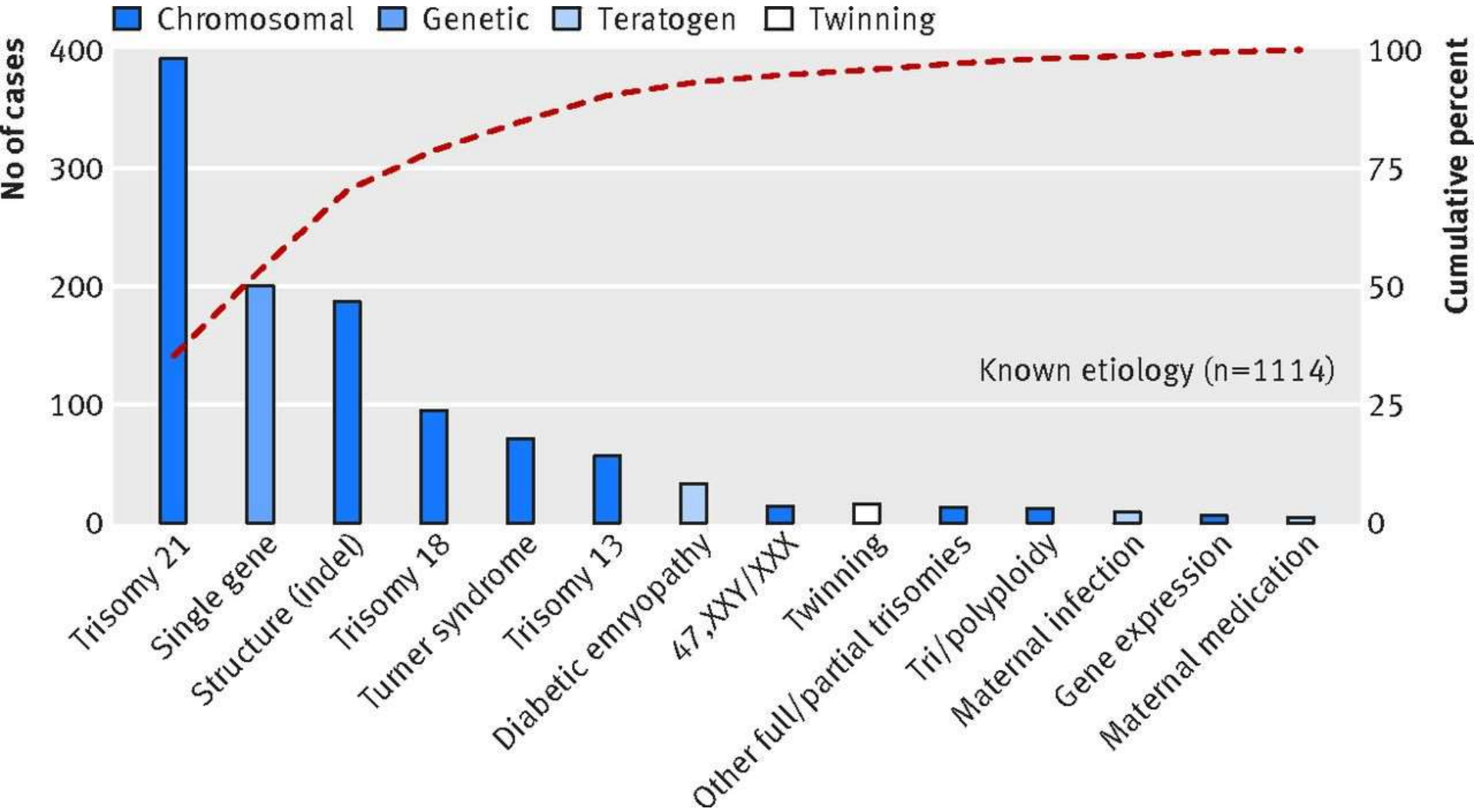
Diseases of childhood

- (1) the neonatal period (the first 4 weeks of life),
- (2) infancy (the fi rst year of life),
- (3) age 1 to 4 years, and
- (4) age 5 to 14 years.

Malformations, disruptions, deformations, sequences, and syndromes

- **Malformations** represent primary errors of morphogenesis, in which there is an intrinsically abnormal developmental process.
- **Disruptions** result from secondary destruction of an organ or body region that was previously normal in development; thus, in contrast to malformations, disruptions arise from an extrinsic disturbance in morphogenesis.
- **Deformations,** like disruptions, also represent an extrinsic disturbance of development rather than an intrinsic error of morphogenesis.
- **A syndrome** is a constellation of congenital anomalies, believed to be pathologically related, that, in contrast to a sequence, cannot be explained on the basis of a single, localized, initiating defect.

Syndromes


Chromosomal
Genetic
Teratogen
Twinning
No of cases
400
300
200
100
0
Cumulative percent
100
75
50
25
0
Known etiology (n=1114)
Trisomy 21
Single gene
Structure (indel)
Trisomy 18
Turner syndrome
Trisomy 13
Diabetic emryopathy
47,XXY/XXX
Twinning
Other full/partial trisomies
Tri/polyploidy
Maternal infection
Gene expression
Maternal medication

Disorders of Prematurity

- Infants born before normal gestation period
- weight 2300 gm and term 34 weeks of gestation
- respiratory distress syndrome [RDS]
- transient hyperbilirubinemia

Therefore, a system of classification that takes into account both birth weight and gestational age has been adopted. Based on birth weight, infants are classified as being

- • Appropriate for gestational age (AGA)
- • Small for gestational age (SGA)
- • Large for gestational age (LGA)

Perinatal group	Neonatal criteria
Full Term Infants (FT)	Full Term >37 weeks gestation, medically and neurologically healthy
Healthy Preterm (HPT)	Premature (<37 weeks gestation), no medical/neurological complications
Medical Preterm (MPT)	Premature, with neonatal medical illness (BPD, RDS, sepsis, NEC, Grade I & II IVH)
Neurological Preterm (NPT)	Premature, with neonatal neurological illness (Grade III & IV IVH, meningitis, shunted hydrocephalus)
Small for Gestational Age Preterm (SGA)	Premature, SGA (birth weight for gestational age below 10th percentile)

BPD = bronchopulmonary dysplasia; RDS = respiratory distress syndrome; NEC = necrotizing enterocolitis; IVH = intraventricular hemorrhage.

Disorders of Prematurity

- Prematurity, defined by a gestational age less than 37 weeks, is the second most common cause of neonatal mortality, behind only congenital anomalies.
- ***Preterm premature rupture of placental membranes* (PPROM):**
- Intrauterine infection:
- ***Uterine, cervical, and placental structural abnormalities***

- • Hyaline membrane disease (Neonatal respiratory distress syndrome)
- • Necrotizing enterocolitis
- • Sepsis
- • Intraventricular hemorrhage
- • Long-term complications, including developmental delay.

Neonatal Respiratory Distress Syndrome (RDS)

- There are many causes of respiratory distress in the newborn, including excessive sedation of the mother, fetal head injury during delivery, aspiration of blood or amniotic fluid, and intrauterine hypoxia brought about by coiling of the umbilical cord about the neck.

Morphology.

- The lungs are distinctive.
- Normal size, they are solid, airless, and reddish purple, similar to the color of the liver, and they usually sink in water.
- Microscopically, alveoli are poorly developed, and those that are present are collapsed.
- When the infant dies early in the course of the disease, necrotic cellular debris can be seen in the terminal bronchioles and alveolar ducts.
- The necrotic material becomes incorporated within eosinophilic hyaline membranes lining the respiratory bronchioles, alveolar ducts, and random alveoli. The membranes are largely made up of fibrin.
- In infants who survive more than 48 hours, reparative changes occur in the lungs.

Perinatal Infections

- two primary routes—transcervically (also referred to as ascending) or transplacentally (hematologic).
- Occasionally, infections occur by a combination of the two routes in that an ascending microorganism infects the endometrium and then the fetal bloodstream via the chorionic villi.

TORCH

- T – Toxoplasmosis
- O – Other infections (Syphilis, varicella zoster, Hepatitis-B)
- R – Rubella
- C – Cytomegalovirus
- H – Herpes simplex t.2

Sudden Infant Death Syndrome (SIDS)

- “the sudden death of an infant under 1 year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history.”
- Thus, SIDS is a disease of unknown cause.

Tumors and Tumor-like Lesions of Infancy and Childhood

- BENIGN TUMORS AND TUMOR-LIKE LESIONS
- MALIGNANT TUMORS

BENIGN TUMORS AND TUMOR-LIKE LESIONS

- Any tumor may be encountered in children,
- but within this wide array we need to mention hemangiomas, lymphangiomas, fibrous lesions, and teratomas.
- The most common neoplasms of childhood are so-called soft-tissue tumors of mesenchymal derivation.

MALIGNANT TUMORS

- Cancers of infancy and childhood differ biologically and histologically from their counterparts occurring later in life. The main differences, some of which have already been alluded to, include the following:
- • Incidence and type of tumor
- • Relatively frequent demonstration of a close relationship between abnormal development (teratogenesis) and tumor induction (oncogenesis)
- • Prevalence of underlying familial or genetic aberrations
- • Tendency of fetal and neonatal malignancies to regress spontaneously or cytodifferentiate
- • Improved survival or cure of many childhood tumors, so that more attention is now being devoted to minimizing the adverse delayed effects of chemotherapy and radiation therapy in survivors, including the development of second malignancies

Common Malignant Neoplasms of Infancy and Childhood

0 to 4 Years	5 to 9 Years	10 to 14 Years
Leukemia	Leukemia	
Retinoblastoma	Retinoblastoma	
Neuroblastoma	Neuroblastoma	
Wilms tumor		
Hepatoblastoma	Hepatocellular carcinoma	Hepatocellular carcinoma
Soft-tissue sarcoma (especially rhabdomyosarcoma)	Soft-tissue sarcoma	Soft-tissue sarcoma
Teratomas		
Central nervous system tumors	Central nervous system tumors	Osteogenic sarcoma
	Ewing sarcoma	Thyroid carcinoma
	Lymphoma	Hodgkin disease

Leukemia incidence:4.1 cases/100,000 children < 15 years

ALL most common; 2000 cases/year (we see 30-40 cases/year)

AML @ 500 cases/year (we see ~6)

CML < 100 cases/year, and CLL not seen

JMML even less common

Typically presents with s/s of anemia, fever, bone pain, bleeding/bruising, HSM/LAD (less in AML; large spleen in CML)

Probable genetic component based on twin studies; linked to trisomy 21, Fanconi, p53 mutations, Bloom, AT, ionizing radiation, and benzene

Hodgkin lymphoma

Wilm's tumor

	NWTSG/COG	SIOP
Low risk	Mesoblastic	Mesoblastic nephroma Cystic partially differentiated
Intermediate risk	Favorable histology	Nonanaplastic Focal anaplasia
High risk	Anaplastic Clear cell sarcoma Rhabdoid	Diffuse anaplasia Clear cell sarcoma Rhabdoid

COG, Children's Oncology Group; NWTS, National Wilms Tumor Study; SIOP, Société Internationale d'Oncologie Pédiatrique.

Stage	Criteria
Stage I	Confined to kidney Complete excision with renal capsule intact and negative resection margins Lymph nodes negative for Wilms tumor spread
Stage II	Regional extension beyond kidney capsule, but confined to flank May include: Tumor penetration through capsule but confined to Gerota's fascia Infiltration into renal vein Complete excision with negative resection margins Lymph nodes negative for Wilms tumor spread
Stage III	Residual tumor, but confined to abdomen May include: Regional lymph node involvement Peritoneal contamination: Biopsy Pre- or intraoperative tumor rupture Tumor growth through peritoneal surface Positive resection margins
Stage IV	Distant metastases: Lung, liver, bone, brain
Stage V	Involvement of bilateral kidneys at diagnosis

Adapted from Davidoff (2012) [4].

Sarcomas of childhood

Infant tumors	Childhood tumors	Puberty tumors
Hemangioma	Childhood leukemia (ALL and AML)	Hodgkin's lymphoma
Infant neuroblastoma	Childhood astrocytoma	Gonadal germ cell tumors
Congenital germ cell tumors	Nephroblastoma (Wilms tumor)	Ewing sarcoma
Infant leukemia (ALL and AML)	Childhood neuroblastoma	Osteosarcoma
Infant (SHH type) medulloblastoma	Embryonal rhabdomyosarcoma	DSRCT
Atypical teratoid/rhabdoid tumor	Langerhans cell histiocytosis	Synovial sarcoma
Central PNET	Non-Hodgkin's lymphoma	Alveolar rhabdomyosarcoma
Ependymoblastoma	Fibromatosis	Neuroblastoma of adolescents and young adults
Hepatoblastoma	Group A posterior fossa ependymoma	Medulloblastoma (SHH type of young adults)
Retinoblastoma		Group B posterior fossa ependymoma
Mesoblastic nephroma		
Congenital fibrosarcoma		
Inflammatory myofibroblastic tumor		
Pulmonary pleuroblastoma		

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; DSRCT, desmoplastic small round cell tumor; PNET, primitive neuroectodermal tumor; SHH, sonic hedgehog homolog.

CNS tumors of childhood