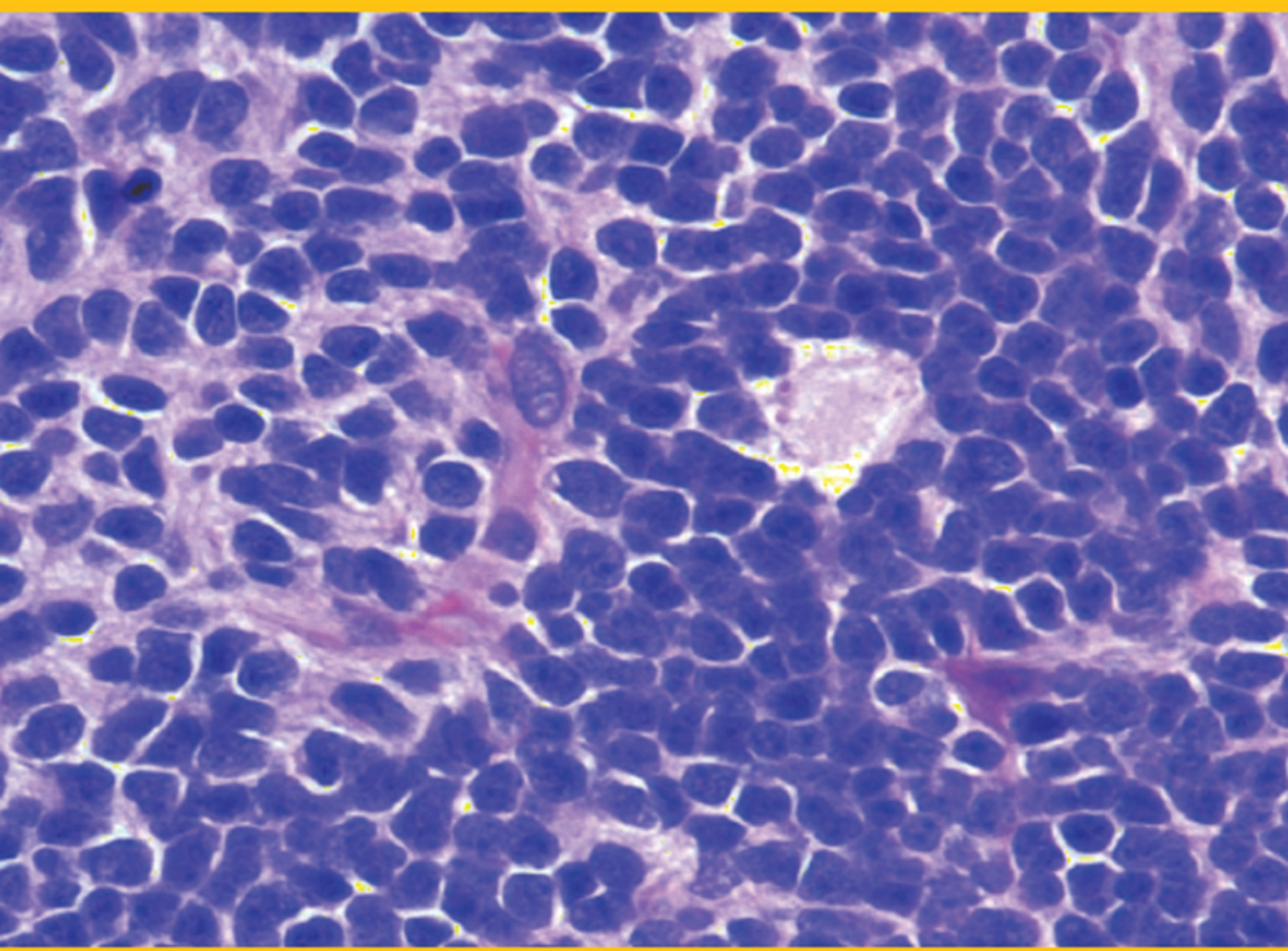
PEDIATRIC PATHOLOGY

A Course Review



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To my husband, Ashok, who is the *Wind Beneath My Wings*

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Preface

This course review book is an assimilation of the comprehensive, yet concise notes that I made for myself as a study guide for board exam preparation (during the year of my fellowship in pediatric pathology). Later, I supplemented those notes with the experience I gained during my 5 years of practice as a pediatric pathologist. The pages that follow cover most of the major topics in pediatric pathology including the embryo, fetal, perinatal, infant and child developmental organ system, and pediatric hematopathology. A chapter on selected topics of pediatric blood transfusion and coagulation is enclosed. Readers will find two separate glossaries embodied in the book (one each for developmental and organ system pathology), which provides alphabetically arranged important terminology with explanations. In addition, I have included a self-assessment section with a quiz containing 115 select cases in anatomic and hematopathology with photomicrographs for each. The correct diagnosis appears at the end of each question. These are mostly spot diagnoses and will help in preparation for the glass slides and the practical part of the examination.

This book is in an outline format, and while by no means can it replace any of the existing excellent pathology textbooks, it is a good resource for pathologists in training, especially pediatric pathology fellows and residents in anatomic and hematopathology, who are preparing for their board examinations. It may also serve as a quick reference guide for pathologists in practice as well as for medical students who are interested in making pathology their career choice.

I have learned from my own personal experience that after you have studied the excellent textbooks in pediatric pathology over the year of your fellowship training, this review course can serve as an outstanding study guide during the last few weeks, days, and hours before the board exams. The handy size and the outline format help keep all the important facts and details fresh in the minds of young pathologists in training, especially during the long airplane journey, sometimes tedious airport delays, and the hotel stay, in the days preceding the board exams.

Any feedback from readers is most welcome. Every effort has been made to keep the book as accurate and precise as possible; however, I would love to hear of important omissions or errors that have slipped into the text, so that together we can improve the quality of this material.

Glossary: Developmental and Fetal Pathology

Acute intrapartum twin-to-twin transfusion: Larger recipient twin is anemic and the smaller donor twin is plethoric

Alagille syndrome: Mutation of *JAG1* gene, del(20p). Intrahepatic bile duct paucity, neonatal jaundice

Algor mortis: Postmortem cooling of the body. Infants/children cool more quickly. Internal organs reach ambient temperature within 18–24 hours

Alkaptonuria: Accumulation of homogentisic acid, pigmented cartilage

Alpha-mannosidosis: Vacuolated lymphocytes in peripheral blood

Amnion nodosum: Fetal surface nodules, pinpoint in size, composed of fetal squames, vellus hair, fibrin, and fibroblasts. Related to oligohydramnios

Amniotic rupture sequence (ARS): Sporadic condition and does not recur. Distinguished from malformations in syndromic setting; clefts do not follow anatomic lines of closure, asymmetrical lesions, abnormal amnion attachments, strands, entanglements. Amniotic surface of placenta may be necrotic/absent, reactive granulation tissue in chorion. Anomalies include encephalocele, body and facial clefts, constrictor ring (Streetor band)

Amoebiasis: Multiple flask-shaped ulcers in colon with extensive necrosis, minimal inflammatory reaction, phagocytosed erythrocytes. Hepatic abscess has anchovy paste appearance. Phase contrast microscopy of a wet stool sample to detect organisms with ingested erythrocytes

Anencephaly: Open neural tube in cephalic region, absent cranial vault, bulging of eyes, exposed degenerating neural tissue in skull floor

Angelman syndromes: del(15), developmental delays, neurological problems, seizures, happy puppet, frequent/unexpected laughter

Apert syndrome: Craniosynostosis, midline hypoplasia, symmetric syndactyly of hands and feet, hearing loss

Atavism: Rudimentary development of an anatomic structure known to have been present in the phylogenetic ancestor, anatomic structure/trait reappearing that had disappeared generations back, e.g., vestigeal tail

Autosomal recessive polycystic kidney disease: Bilateral kidney enlargement and retention of fetal lobulation, elongated cysts of collecting ducts, associated congenital hepatic fibrosis

BAPP: β-amyloid precursor protein stain confirms the hypoxic/traumatic axonal injury pattern

Battledore placenta: Marginal cord insertion in the placenta—associated with hypercoiling and stillbirth

Beckwith-Weidemann syndrome: Large body size, hemihypertrophy, large organs, umbilical hernia, macroglossia, grooves on ear lobule, cytomegaly of adrenal cortex, Wilms tumor

Bone in rickets: Growth plate shows abundant osteoid that may extend into the metaphysis, fragmentation and fraying of epiphysis on x-ray. Skull has ping-pong ball sensation on touching away from the suture lines (craniotabes)

Brain in Down syndrome: Neurofibrillary tangles similar to Alzheimer brain

Branchial arch syndromes: Hemifacial microsomia, Goldenhar syndrome, and Treacher Collins syndrome

***C-Kit* gene:** Encodes tyrosine kinase that is required for melanoblast migration

Campomelic syndrome: Bent femurs

***Candida albicans* infection:** Rounded white spots (1–2 mm) on the umbilical cord

Cat eye syndrome: Trisomy 22p, downslanting palpebral fissures, hypertelorism, ocular coloboma, preauricular skin tags/pits

Cebocephaly: Most extreme variant, single median eye with varying duplication of intrinsic ocular structures, arrhinia, and proboscis (protrusion from forehead) formation; noted with alobar holoprosencephaly

Cephalhematoma: Accumulation of blood between skull and external periosteum. Confined by the sutures of skull bones

Cephalocele: Herniation of brain or meninges through a defect in the skull

Chagas disease: *Trypanosoma cruzi* in fetal vessels in the villi of placenta, giant cell transformation

Chain of custody: Procedure established to verify the possession of an object from the time it is collected until it is offered into evidence in court

CHARGE association: Coloboma, heart defects, choanal atresia, mental retardation, genital hypoplasia, ear anomalies

Chignon: Circumscribed area of edema and hemorrhage in the vertex of skull—due to suction facilitated delivery

Child abuse prevention and treatment act (P.L 93-247): Abuse and neglect are defined as, "the physical or mental injury, sexual abuse, negligent treatment, or maltreatment of a child under the age of 18 by a person responsible for the child's health or welfare under circumstances which indicate that the child's health or welfare is harmed or threatened thereby."

Confined placental mosaicism: Survival advantage to the trisomic zygote

Congenital gigantism of toes: Neurofibromatosis

Congenital syphilis: Hydrops fetalis, pneumonia alba with gummatous necrosis, osteochondritis, enchondritis, morbilliform rash on skin

Conradi-Hunermann syndrome: Chondrodysplasia punctata of patella

Craniosynostosis: Premature fusion of one or more sutures of skull. Most mutations for major craniosynostosis syndromes are on *FGFR2*

Crouzon syndrome: Craniosynostosis, maxillary hypoplasia, shallow orbits, and ocular proptosis

Currarino syndrome: AD disorder. The triad includes partial sacral agenesis, presacral tumor (anterior meningocele, enteric cyst, or teratoma) and anorectal malformation. S1 and half of remaining sacrum is spared giving rise to "scimitar sign" on imaging. Mutations in *HLXB9* gene

Cystinosis: Cystine crystals, kidney shows glomerular sclerosis, hyalinization and fibrosis

Cytogenetics of complete mole: Diploid XX or XY; all paternal

Cytogenetics of partial mole: Triploid XXY, XXX, XYY; paternal and maternal

Death cases that need to be reported to the medical examiner/coroner: All sudden/unexpected deaths, all child deaths outside hospital, deaths in emergency room, and all unnatural deaths

Death due to drowning: Hemorrhage of petrous bone

Deformation and disruption: Extrinsic interruption of normal development

Diffuse chorioamnionic hemosiderosis: Complication of circumvallate membrane insertion—due to persistent marginal bleeding

DiGeorge syndrome: Velocardiofacial syndrome, del(22q11.2). Parathyroid hypoplasia/aplasia, hypocalcemia, thymic hypoplasia, outflow tract anomalies of heart and anomalies of lower face

Dysplasia and malformation: Intrinsic abnormalities of primordium

Elfin facies: Williams syndrome, idiopathic hypercalcemia

Epiglottitis: Secondary to *Haemophilus influenzae* infection

Erb palsy: Injury to the fifth and sixth cervical roots of brachial plexus. Traumatic delivery related

Exstrophy of bladder: Risk of development of neoplasia of bladder several decades after birth

Farber disease: Multiple skin nodules

Fetal alcohol syndrome: Telecanthus, absent philtrum and thin vermillion border of upper lip

Flow cytometry: Useful in perinatal pathology in two scenarios: diagnosis/typing of congenital leukemias and in the classification of suspected triploidy/tetraploidy. Performed on the dissociated cells of fetus or placenta

Fragile X syndrome: *FMR-1* gene, CGG nucleotide repeat. Large floppy ears, macroorchidism, mental retardation

Friderichson-Waterhouse syndrome: Fulminant infection with *Haemophilus influenzae* and *Neisseria meningitides*, hemorrhagic infarction of bilateral adrenal glands

Gastroschisis: Premature ablation or disruption of omphalomesenteric artery

Gaucher cells: Histiocytes in bone marrow have "crinkled tissue" appearance due to cytoplasmic striations

Goldenhar syndrome: Malformed ear, micrognathia, bilateral cleft lip/palate, agenesis of thumb

Group B streptococcal (GBS) pneumonia: Mimics hyaline membrane disease in preterm infants. Gram-positive bacterial colonies in the membranes

GSD type II: EM; dense lysosomes filled with glycogen

GSD type IV: Storage material in the cells is diastase resistant, pectinase labile

Hanhart complex: Oral involvement, micrognathia and limb defects

Hemifacial microsomia: Abnormal ear, asymmetric jaw

Hemosiderosis of liver: Iron overload. Iron staining confined to Kupffer cells and there is no tissue damage

Holoprosencephaly: Developmental defect with impaired midline cleavage of embryonic forebrain. Graded into alobar, semilobar, and lobar types

Homicidal suffocation: Pulmonary siderophages may be seen

Hurler syndrome: MPS type I, coarse facial features, prominent supraorbital ridges and depressed nasal bridge

Hyperthermia: Core body temperature greater than 40°C

Hypothermia: Core body temperature lesser than 35°C

Immediate cause of death: Complication of the initial disease or injury that ultimately leads to death

Infants born to diabetic mothers: Macrosomic, pancreatic islets are enlarged with large hyperchromatic beta cells, calcified thrombi in renal veins

Intervillous space: Preservation of intervillous space in massive perivillous fibrin deposition while in placental infarction the perivillous space is collapsed

Jeune thoracic dystrophy: Asphyxiating thoracic dystrophy, very small thorax, and extreme pulmonary hypoplasia. Lethal in infancy

Klinefelter syndrome: 47, XXY, tall males with gynecomastia and arachnodactyly. Testes have atrophic tubules and hyperplastic clusters of Leydig cells

Klumpke paralysis: Injury to the seventh and eighth cervical roots and the first thoracic nerve root. Traumatic delivery related

Krabbe disease: Globoid cells in white matter leukodystrophy, demyelination of nerve cells

Lesch-Nyhan syndrome: Hyperuricemia, gouty arthritis, choreoathetosis, spasticity and self-mutilation

Limb body wall complex: Vascular disruption believed to be the cause. Marked deformation of fetus including thoracoschisis, abdominoschisis, facial cleft, severe scoliosis, pseudoencephalocele, internal structural anomalies, short umbilical cord with placenta adherent to viscera

Lisch nodules of iris of eye: Neurofibromatosis

Livor mortis: Postmortem purple discoloration of skin and internal organs that develops in the dependent portions of the body. It is deep-purple red in asphyxia deaths and bright cherry-red in deaths due to carbon monoxide/cyanide poisoning/snow

LSD-induced embryopathy: Skeletal defects and microcephaly

Maceration: Retained dead fetus in utero; skin slippage, heme staining of skin, relaxation of autolyzed muscles

Malformation syndromes: Mandelian or chromosomal in origin

Manner of death: The circumstance under which death occurred. Five types: natural, accidental, homicide, suicide, and undetermined

Marfan syndrome: Dislocation of lens of eye, cystic medionecrosis, dissection of aortic wall

Mechanism of death: Physiological derangement or biochemical disturbance (produced by the cause of death) that is incompatible with life

Meckel-Gruber syndrome: Abdominal distension due to renal multi-cystic dysplasia, encephalocele, polydactyly of hands and feet

Menkes syndrome: *ATP7A* gene involved. X-linked recessive trait. Defect in intestinal copper absorption with low serum levels of copper and ceruloplasmin. Child has coarse kinky hair (pili torti)

Mesenchymal dysplasia: Anomalous villous stromal development. Hydropic chorionic villi, villous cisterns, stromal hypercellularity, generalized villous hypovascularity. Beckwith-Wiedemann syndrome may be associated

Metachromatic leukodystrophy: Accumulation of cerebroside sulfate, EM of white matter neuron; prismatic/tuffstone inclusions

Minor abnormalities of Down syndrome: Epicanthal folds, anteverted nares, single palmer crease, clinodactyly (absent middle crease) of fifth finger

Molar triploidy: Diandry, paternal origin, symmetrical IUGR, partial hydatidiform molar placenta

Monoamniotic twins: Cord complications include cord knots, entanglements, cord braiding, leading to asphyxia of fetuses

Monozygotic twins: Display discordance for major malformations

Neonatal hemochromatosis: AR, advanced congenital cirrhosis, iron overload in hepatocytes. Less involvement of biliary epithelium and Kupffer cells

Neurenteric cysts: Congenital cysts intraspinal and extramedullary found in contact with CNS. Lined by GI mucosa

Neurogenic arthrogryposis: Due to exposure to hyperthermia in early gestation

Neuronal ceroid lipofuscinosis: EM; granular osmiophilic deposits, curvilinear bodies, fingerprint profiles

Niemann-Pick disease: Histiocytes in bone marrow have "soap bubble" appearance of cytoplasm

Non-molar triploidy: Digyny, maternal origin, severe asymmetrical IUGR, syndactyly of fingers and toes, non-molar hypoplastic placenta

Non-disjunction: Failure of homologous chromosomes or sister chromatids to segregate properly during cell division

Oculocerebrorenal syndrome of Lowe: Hydroureters and hydronephrosis. Congenital cataract, metabolic acidosis, and mental retardation

Otocephaly: Extreme mandibular hypoplasia, microstomia, and synotia

Parvovirus B19 inclusions: Found in fetal erythroid precursors. Amphophilic inclusions displace chromatin to the nuclear margin and cells are enlarged

Pentalogy of Cantrell: Due to abnormal development of septum transversum during fourth week of development. Clefting/agenesis of distal sternum, diaphragmatic hernia, midline ventral abdominal defect/omphalocele, defective apical pericardium and its communication with peritoneal cavity, ectopia cordis