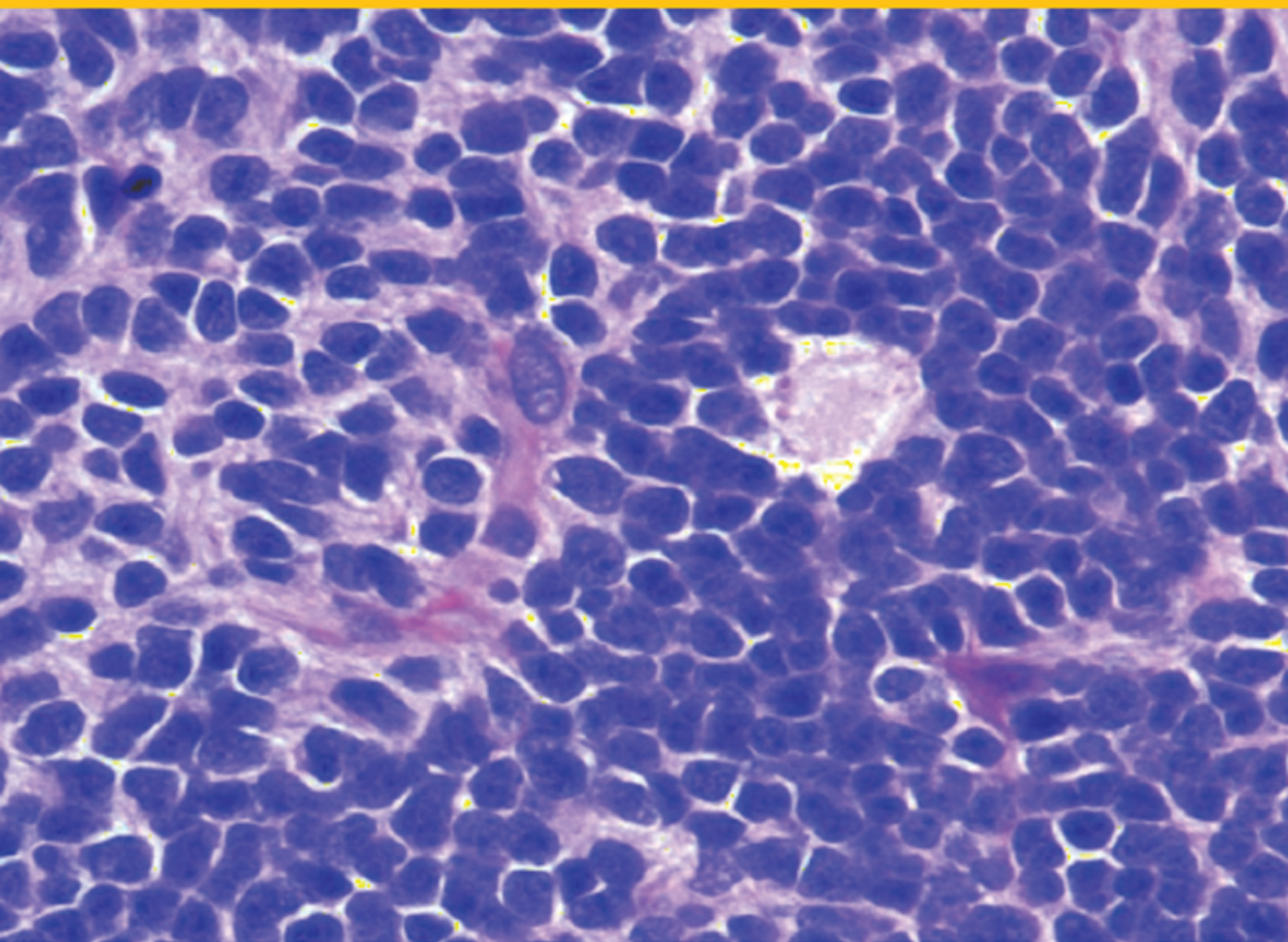


# PEDIATRIC PATHOLOGY

## A Course Review



**Shipra Garg**



**CRC Press**  
Taylor & Francis Group

# Pediatric Pathology

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# Pediatric Pathology

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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.



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# 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 (Streeter 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., vestigial tail
- Autosomal recessive polycystic kidney disease:** Bilateral kidney enlargement and retention of fetal lobulation, elongated cysts of collecting ducts, associated congenital hepatic fibrosis
- BAPP:**  $\beta$ -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, down-slanting 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 vermilion 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 meningitidis*, 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:** Macroscopic, 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:** Mendelian 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 palmar 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 arthrogyrosis:** 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. Clefing/agenesis of distal sternum, diaphragmatic hernia, midline ventral abdominal defect/omphalocele, defective apical pericardium and its communication with peritoneal cavity, ectopia cordis