The Pediatric Autopsy in Africa

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• ***Context.***—**Within the continent of Africa few countries have been able to practice pathology at the levels present in Europe and the Americas, and pediatric pathology does not exist as a stand-alone specialty. The author was invited by a colleague from Harvard Medical School, Boston, Massachusetts, to join a group of North American pathologists in presenting a course on the Contribution of Anatomic Pathology for advancing the health of women and children in Africa. The course was held in Ethiopia in June 2011, to review the current state of pediatric pathology in Africa and to provide resources/teaching for improving pediatric pathology services in low-resource settings.**

Objective.—**To provide a succinct description of applicable autopsy techniques and the interpretation of gross, microscopic, and ancillary findings with respect to Africa's need to enhance the health of women and children. The author makes suggestions for obviating possible problems in anticipation of increased demands by national authorities and of public expectations of pathologists who usually have had only general training.**

Data Sources.—**This article is based upon the author's personal experience of practicing pathology in Africa for the past 51 years, which has included visiting pathology laboratories in 9 African countries and interacting with colleagues in 18 additional African countries. The contents of this article are derived from personal observations, recent publications, and information gleaned from Internet sources.**

Conclusions.—**Even without specific training in pediatric pathology, it is possible for pediatric autopsies to be undertaken in Africa and other resource-poor settings, in a manner that facilitates sound decision making for improving the health of women and children.**

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There are several published textbooks[1–6] that describe how pediatric autopsies should be undertaken and adapted for particular circumstances. This article attempts to describe methods that are appropriate for general pathologists who practice in Africa and have not received specific training in pediatric autopsy techniques. These suggestions are adaptable to any resource-poor setting and are useful for application by any pathologist with any level of training. Africa has the highest maternal, perinatal, and infant mortality rates in the world, and unfortunately, these have not changed significantly in the past 2 decades. *Much effort and resource expenditures have gone into addressing underlying socioeconomic, educational, cultural, and environmental factors without having given adequate attention to the skills and facilities needed to make accurate diagnoses upon which appropriate interventions should be made*. It therefore is essential that pediatric autopsies be undertaken by appropriately skilled pathologists having access to affordable resources and who can be confident that health care decision makers will use their diagnoses. In Africa the role of pathologists in the overall care of health is not nearly as valued by health care administrators and clinicians as it is in industrialized countries. As a result, few medical students choose pathology as a specialty; therefore, the few pathologists in service are vastly overextended. As respect for pathologists is low among clinicians, utilization of pathology services is minimal and when used, clinician input is often absent; thus, service is compromised. For example, pathologists are often called upon to undertake diagnostic procedures and autopsies with minimal clinical information or cooperation in obtaining appropriate consent. This results in suboptimal diagnoses and reinforces clinician disrespect. This situation can be obviated with improved interaction in the form of conferences in which pathologists not only attend but also present pathologic findings.

The problem of low resources includes the paucity of professionals in all specialties of pathology. Some relatively simple solutions should be considered. Advancing use of nonprofessional assistants can be used to improve time management for the pathologist. For example, when a highly trained laboratory scientist is the senior mortician, the initial procedures for securing autopsy consent, obtaining essential clinical data, coordinating the intended day and time of the funeral, recording external measurements and body weight, and taking relevant swabs (usually microbiologic), photographs, and x-rays may be performed before the pathologist even enters the mortuary.

Pediatric autopsy procedures should be undertaken with a clear understanding of the purpose for doing so in each

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individual case. Relevant background information is essential. Irrespective of the laws of nations, global ethical standards expect fully informed consent to be provided in nonstatutory cases, but excessively detailed consent forms stifle procurement. Consent may effectively be obtained by an experienced mortician, who is fully acquainted with the various autopsy procedures undertaken by pathologists. When such a person patiently explains the value of autopsies to families and the public at large, and is able to fully answer questions and give assurances of nondisfigurement, trust and support from the community are facilitated.

In this article I provide and discuss procedures for detailed external and internal postmortem examination. These are to be guided by an ethos of accuracy and attention to detail in a background of basic knowledge of common congenital anomalies and childhood maladies. Useful routine methods for removing the brain in very young infants and stillbirths are provided. The recording of autopsy findings and the interpretation thereof with respect to stages of developmental maturation and any preceding stress or illness are presented. The importance of routinely sampling specific anatomic sites, such as the larynx with its vocal cords cut transversely, costochondral junction, thymus, adrenal glands, kidneys, lungs, and particular regions of the central nervous system, for the purpose of obtaining vital information is too often overlooked. The final report should include the results of all ancillary tests, an interpretation of the sequence of events that led to death, and any health care issues that should be addressed within the family, the profession, or the community.

REASONS AND BENEFITS FOR UNDERTAKING AUTOPSY EXAMINATIONS

Relative to the situation in industrialized countries, there is still a relatively low incidence of litigation in medical practice throughout Africa. Nevertheless, Africa's pathologists should be aware that the rate of litigation is rising and that they will, with increasing frequency, be called upon to undertake an important role in settling such disputes. It therefore is important for us to be fully aware of the general purpose of performing autopsies as well as the specific reason for undertaking each individual postmortem examination:

1. In teaching hospitals the most common reason is to confirm or to elucidate the clinical diagnosis while simultaneously teaching undergraduate and postgraduate students.
2. Autopsies also have an important role in research and in our understanding of disease.
3. Autopsies are necessary in quality assurance, in monitoring diverse public and community health matters, and in monitoring familial disease.
4. A factor that is often overlooked is the procurement of normal control tissues for diagnosis and research.

PRELIMINARY PROCEDURES

In Africa, pathologists, who are usually trained as generalists, are called upon to undertake a wide spectrum of pathologists' activities while having very limited access to resources. These activities will increasingly include the undertaking of forensic autopsies with limited background information or specific in-depth training. The importance of obtaining a preautopsy clinical diagnosis; of having a clear reason for doing the autopsy within the context of hospital practice; of considering environmental, hereditary, and iatrogenic issues; and of recognizing public health and legal matters cannot be overemphasized. Most African countries provide widespread antenatal care and early childhood development monitoring facilities from where concise clinical data may be sourced. The most useful data for the pathologist relate to prenatal maternal history, gestational age, the birth process, birth weight, and postnatal growth and development.

CONSENT

Irrespective of the laws of different countries with regard to consent for undertaking an autopsy, there is an international ethical code for obtaining fully informed consent in all nonstatutory autopsies.

Obtaining informed consent presupposes that the person obtaining the consent is fully aware of what happens in the mortuary when an autopsy is performed. There are issues relating to how much should be explained and how detailed the consent should be, but fears of body disfigurement should be allayed and religious issues should be fully respected. The person giving the consent should be made aware that organs are removed from the body, weighed, cut, and dissected. Small portions of tissue are removed for microscopic examination after formalin fixation and processed to form paraffin-embedded blocks and from them, stained slides that are not returned to the body. The role of potential frozen section analysis, biochemistry, genetics, microbiology, radiography, tissue culture, and photography should be explained. It is also proper that the methods for returning organs to the body and what is not returned are explained. Thorough autopsies on newborn infants frequently require retention of the brain and/or heart for special purposes. Such action will often delay the funeral for which an agreement should be arranged in advance of the autopsy. Experience by British pediatric pathologists has shown that when an excessively expanded consent form is used, support for research and teaching activities on autopsy material is often withheld. Ideally, consent should be obtained by the attending physician and a senior, fully trained, and certified mortician capable of explaining procedures and answering questions.

In Africa the quality of mortuary facilities is extremely variable. While it is possible to effectively undertake autopsies with rudimentary facilities, such activity compromises accurate interpretation of findings and facilitates the spread of infection. It should be appreciated that pediatric autopsy procedures require fine dissecting instrumentation as well as additional equipment not often used for adults, such as a magnifying glass and/or a dissecting microscope, a balance able to weigh a tenth of a gram, measuring calipers, and a flexible tape measure.

PEDIATRIC AUTOPSY PROCEDURE

External Examination

External body and organ configurations, size, weight, and relationships should be noted (eg, head circumference normally approximates crown-rump length [sitting height]). In regions in which starvation and malnutrition exist, the autopsy measurements are critical in documenting the extent of such pathologic processes. Reduced weight for age represents protein energy malnutrition, while reduced weight for height represents wasting and stunted growth.

Table 1. External Measures and Body Weight
Crown-heel length
Crown-rump length
Supraorbital head circumference
Chest circumference at nipples
Abdominal girth at umbilicus
Foot length
Limb length of long bones in cases of suspected skeletal dysplasia

The World Health Organization provides charts for normal growth and development in respect of these evaluations.[7] A mid-upper arm circumference less than 115 mm is considered to be a significant indicator of malnutrition in children 6 to 60 months of age.[8]

On the basis of provided clinical data and macroscopic observation, an informed decision is made regarding radiography, external photography, and obtaining cultures for microbes. Even in resource-poor settings without availability of x-rays or without dedicated cameras, the ubiquitous cell phone usually has a camera included and can be used to great benefit if cases require later consultation. Accurate weights and measures are undertaken and compared to published norms. When laboratory scales are not available, fairly accurate measurements may be made by using commercial household balances of the type that are normally used for weighing food/baking ingredients.

When multiple external anomalies are present and do not obviously fall into a recognized syndrome or sequence, guidance can come from the electronic databases without having to depend upon rarely available and expensive karyotyping procedures.

Skin

With respect to skin changes, forensic cases always require detailed recordings of the sites, nature, and dimensions of injuries. Children may have a rash, hemorrhages, bullae, and/or changes in pigmentation. The extent of nappy rash (diaper rash) should always be recorded when present, as it may be an indicator of the quality of home care.

Face and Head

Comment should be made of the face and head structure, the appearance of eyelids and conjunctivae (color, clarity, etc), spacing of eyes, patency of nasal passages, and the structure of lips and the philtrim (intactness, length, tethering, etc.). The mouth should be opened to examine the mucosa, palate, gums, teeth, and tongue. It is useful to examine the auditory canal for the presence of meconium in neonatal deaths and to record external ear structure, rotation, and location. The apparent length and thickness of the neck and extent of the posterior hairline should be commented upon.

Trunk and Extremities

The shape of the chest and spacing of nipples should be recorded as should the abdominal wall, umbilicus, and umbilical cord when still present. The external genitalia and anus should be examined for congenital anomalies and patency. The limbs, feet, hands, digits, and palms must be examined for configuration and crease anomalies.

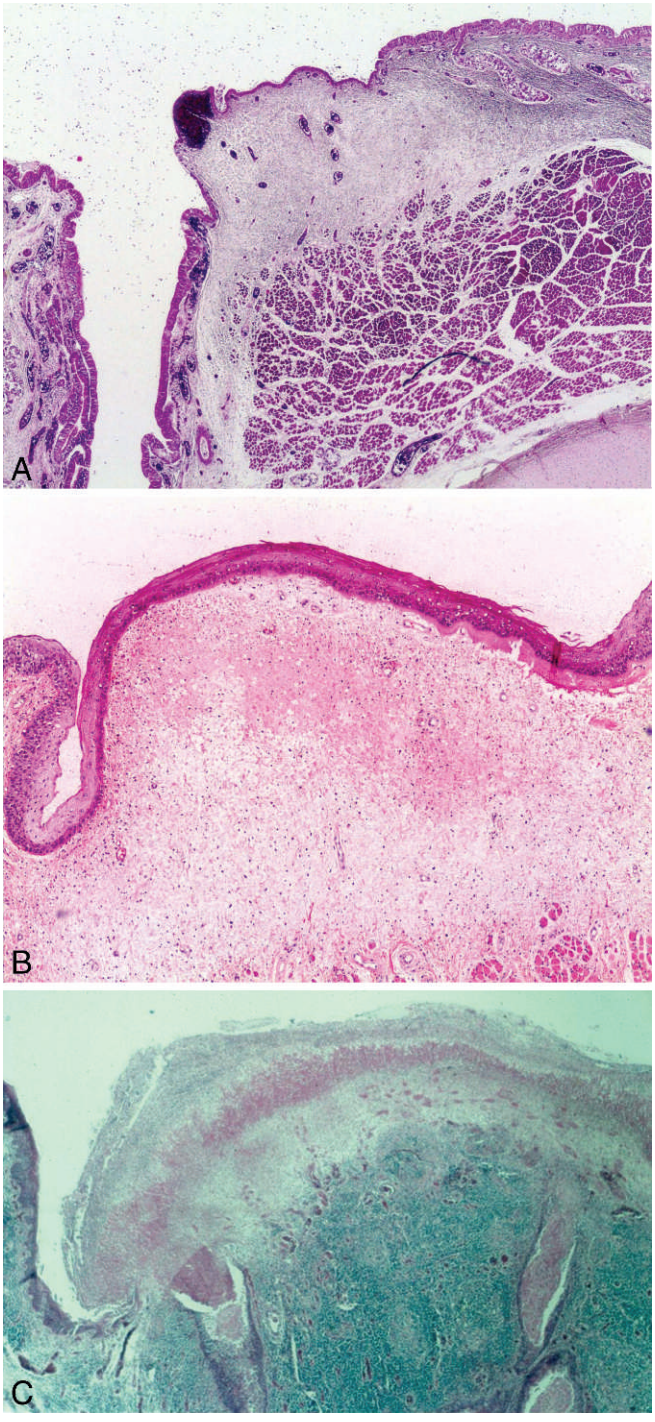


Figure 1. *Sections of larynx. A, Larynx showing hemorrhage just under epithelium with edema in mucosa; case involved choking. B, Edema of larynx, death due to choking. C, Larynx in a lethal case of diphtheria toxin (hematoxylin-eosin, original magnifications ×1 [A] and ×4 [B]; Masson trichrome, original magnification ×4 [C]).*

INTERNAL EXAMINATION

It is prudent to commence the internal dissection with sterile instruments to allow cultures from relevant viscera. In Africa there are significant numbers of children at the extremes of being either undernourished or overnourished. Therefore, it is good practice to routinely measure the thickness of subcutaneous fat on the chest midway between

Table 2. Basic Structure for a Suggested Fetal/Stillbirth Autopsy Template

Basic Structure for a Suggested Fetal/Stillbirth Autopsy Template

Name of mother: …… Hospital Number:……

Address:……..…….

Clinical data:……..……

……..……..……

Name of Autopsy case:…… Sex……Hospital No……

Date & Time of birth:……..……..…Date & Time of death:……..…

Date & Time of Autopsy:……..Postmortem interval:……..…..…

Gestational Age…… Chronological Age:……

Referring Doctor:……. Contact Number/Address:…….

Pathologist:…….Mortician:…….……Witnesses:……..

Consent as per consent form for a full autopsy:

Consent NOT given for:

EXTERNAL EXAMINATION:

Body identified by……Male/female/ambiguous.

Weights and Measures: Whole body weight, Foot length, Crown Heel length, Crown Rump length, Head circumference, Chest circumference at level of nipples, Abdominal girth at umbilicus and length of limb long bone in cases of suspected skeletal dysplasia. In addition the expected weights and measures for gestation or chronological age and/or body length should be provided. Skin Changes. Face and head structure , Eyes and Ears, Nose, mouth and philtrim, Neck and hairline. Chest and spine, Umbilicus and cord, Genitalia and anus.

Upper & lower limbs, Digits and creases.

INTERNAL EXAMINATION:

Organ weights should be recorded and compared with expected for gestation and chronological age or for body length when information is not provided.

Cardiovascular System: Pericardium, Heart configuration & vascular connections & internal structure.

Respiratory System: Pleural cavities& diaphragm, Lungs, Larynx, Trachea and Main Bronchi.

Gastrointestinal System: Tongue, Pharynx, Esophagus, peritoneal cavity, stomach, duodenum, small & large intestines, Liver, Gall bladder and Pancreas. Reticuloendothelial System: Spleen, Lymph Nodes and Thymus. Endocrine System: Thyroid, Adrenals and Pituitary. Genitourinary System: Kidneys, Ureters, Bladder, Urethra and Internal Genitalia. Musculoskeletal System: Skin & Subcutaneous fat, Muscle bulk, Ribs, Vertebrae and Long Bones. Central Nervous System: Scalp &Skull Bones, Meninges, Brain and Spinal Cord.

Viral & Tissue Cultures, Guthrie Card, Biochemical and Toxicological Analyses and Frozen Tissues/Sections.

SUMMARY OF POSITIVE MACROSCOPIC FINDINGS:

PROVISIONAL ANATOMICAL DIAGNOSIS:

HISTOLOGY:

RESULTS OF ANCILLARY TESTS:

FINAL DIAGNOSIS:

FINAL COMMENT:

Name of reporting pathologist, signature and date of issue.

Table 3. Stress Reactions in the Thymus[a]

0–12 h: Parenchymal hemorrhages
12–48 h: "Macrophages" in cortex
48–72 h: "Macrophages" with "mulberries" in cortex, cellularity of cortex begins to diminish
3–7 d: Corticomedullary distinction lost with increasing prominence of Hassall corpuscles
7–14 d: Involution begins whereby lymphocytes appear in increasing numbers in the medulla
>14 d: Advanced involution whereby there is overall relative depletion of lymphocytes and they mainly occupy the medulla

[a] Data derived from Singer et al.[16]

Table 4. Rib Growth Impairment[a]

Impairment	Fetuses/ Infants	Very Young Children
Short chondrocyte columns	12–36 h	12–48 h
Clustering of chondrocytes	24–48 h	36–72 h
Capillary penetration fails	36–72 h	3–7 d
Narrow banding and short bridges	>72 h	7–14 d
Thick matrix and long bridges	>7 d	>14 d

[a] Data derived from Sinclair-Smith et al.[19]
Fetuses refers to a gestation between 30 and 44 weeks and infants to up to 4 weeks postnatal life. Very Young Children refers to an age between one and nine months.

the nipples and on the abdomen midway between the xiphoid process and the umbilicus as rough indicators of nutritional status. In my experience, cases of severe wasting are associated with less than 3 mm of subcutaneous fat in the abdomen and less than 2 mm in the chest, no matter the age of the decedent. In classical kwashiorkor the fat is between 8 and 15 mm on the abdomen and 5 to 12 mm on the chest. For obesity the measurements are more age specific, but for a general rule, more than 25 mm on the abdomen and more than 12 mm on the chest is obese for all ages.[9,10]

Care should be taken to search for commonly occurring congenital anomalies, to take photographs of abnormalities and, depending upon the clinical situation, to obtain cultures from heart blood (or spleen if heart blood is not obtainable), pharynx, bronchi, lung parenchyma, and stools. Biochemical analysis of blood, vitreous humor, urine, and bile may be appropriate for metabolic disorders and toxicologic evaluations, while a blood spot on a Guthrie card can be useful for potential future DNA analysis.

The *chest* should be opened after aspirating the pleural cavities for air to identify a possible pneumothorax that may have occurred during attempted resuscitation. The chest is opened by removing the sternum with cartilaginous rib ends, taking care to sample the costochondral junction (fifth rib) for histologic analysis. The thoracic cavity is best examined before the peritoneal cavity is opened so as to avoid possible contamination by intestinal organisms before taking selective cultures, which routinely should include a main bronchus or pneumonic lung tissue.

After removing the thymus and pericardial sac, the external configuration and vascular connections of the heart are checked while the heart is still in situ. Small probes are useful for checking the systemic and pulmonary venous connections to relevant heart chambers. The heart and lungs may then be eviscerated together with the tongue, pharynx, submandibular salivary glands, esophagus, larynx, and trachea.

Macroscopic examination and sampling of the *larynx and vocal cords* in young infants is too often overlooked, particularly when dealing with sudden unexpected death in infancy (SUDI, formerly SIDS). It is recommended that the intact larynx, trachea, and main bronchi be opened along their posterior surface when internal swabs for culture may also be taken. The larynx is separated with the epiglottis from the cricoid cartilage and trachea just above the thyroid isthmus. The larynx is then bisected longitudinally to prepare tissue samples for histologic analysis. These are cut along the long axis of the trachea and transversely across the vocal cord tendons. The objective is to demonstrate the upper false cord, sulcus, and vocal cord itself with intact surface epithelium and any adherent respiratory tract content.

The internal dissection of the *heart and lungs* should then follow according to individual preferences for recognizing structural abnormalities of the heart chambers, valves, and coronary ostia as well as the origin, course, and size of the great vessels and their branches. It is recommended that at least 1 longitudinal full-thickness section be taken from the posterior aspect of the left ventricle that includes atrium, ventricle, coronary vessels, mitral valve, and a papillary muscle. Lung samples should include representative macroscopic lesions as well as samples from each lobe taken horizontally midway between the hilum and the most distal periphery.

When the *abdominal cavity* is opened, one should check that all the organs are correctly placed and orientated and decide upon whether or not cultures should be taken. Ideally, routine cultures should be taken from turbid peritoneal fluid, abscesses, and rectal stools in cases with diarrheal disease. When there is the potential of an inborn error of metabolism, and in forensic cases, samples of urine, bile, gastric content, and vitreous humor should be taken for biochemical or toxicologic analysis. Depending upon available toxicologic laboratory resources, portions of liver and kidney may also be kept in a freezer pending further analyses until histologic features of zonal necrosis, highly suggestive of possible poisoning, have been verified.

Before removing the intestines from the mesentery in situ, note the presence or absence of intussusceptions, diverticulae, atresias, or incomplete mesenteric fixation, which renders the cecum excessively mobile, with displacement of the vermiform appendix to the right upper quadrant. Also note the presence or absence of spleniculi, ectopias of pancreatic tissue in the gut, ectopias of adrenal tissue on gonads, or displacement of adrenal glands partly through the diaphragm, as these findings are associated with syndromes and/or bleeding complications. In premature boys the location of the testes should be recorded.

Examination of the *central nervous system* involves removal of the brain and the spinal cord from the cranial cavity and the spinal canal. Individual pediatric pathologists and neuropathologists have their preferred methods. It is important to follow a particular routine and to always examine the status of the foramen magnum before opening the skull. The author prefers, as a matter of routine, to remove the brain in 3 parts, followed by anterior removal of the spinal cord, but neuropathologists, particularly when dealing with cases of hydrocephalus, usually prefer to remove the brain with the spinal cord intact and within their bony coverings.[11] Application of this method may require special consent. In the routine method a question

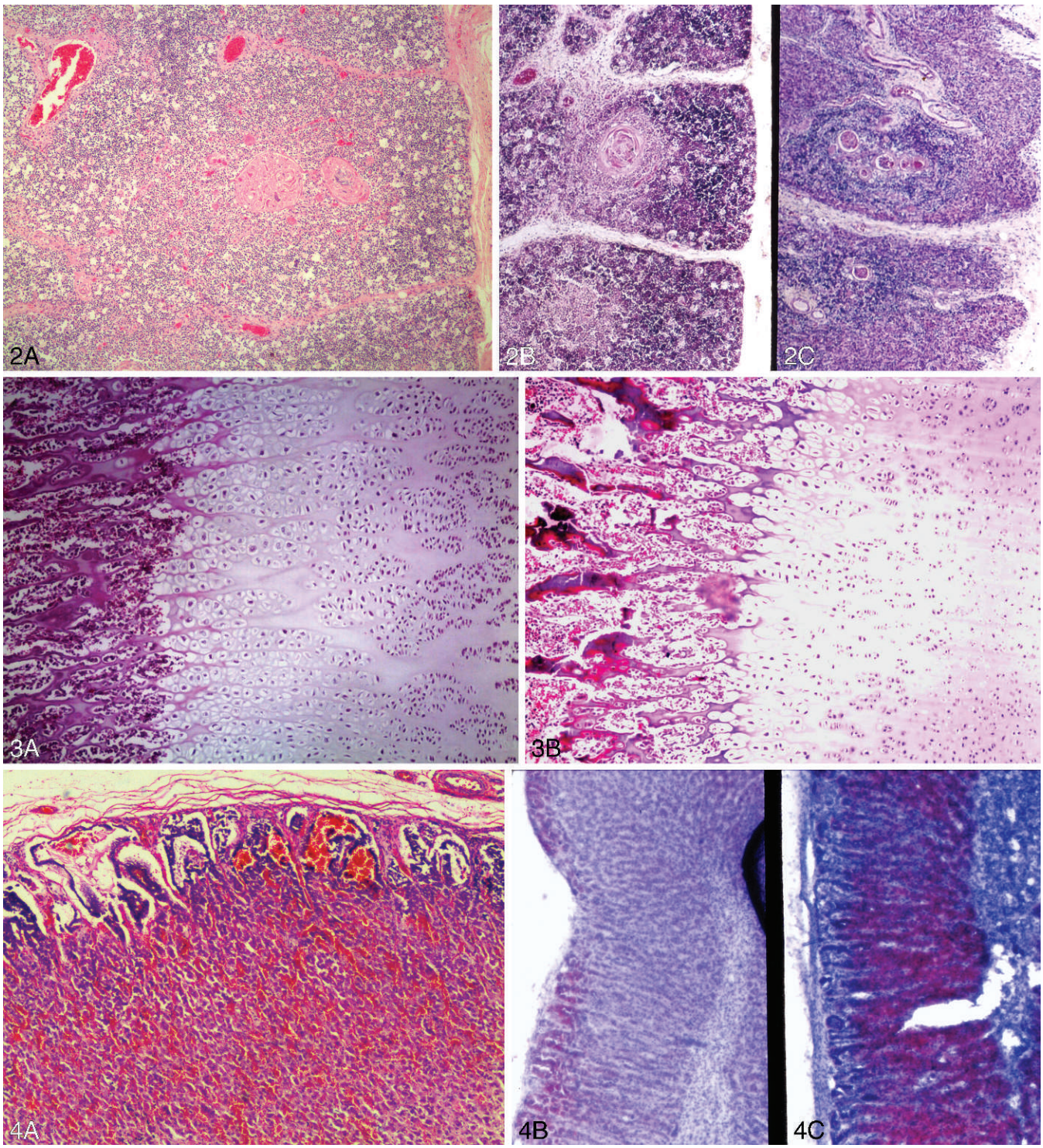


Figure 2. *Thymic involutionary changes. A, Thymic stress of hours' duration with "starry sky" appearance due to histiocytes in the cortex. B and C, Thymus showing stress of several days' duration with loss of corticomedullary distinction, starry sky change, and prominent Hassall corpuscles (hematoxylin-eosin, original magnifications ×4 [A] and ×1 [B and C]).*

Figure 3. *Normal rib histologic features and stress changes. A, Normal rib at costochondral junction from a near-term live birth with normal straight chondrocyte columns and blood vessels at "top." B, Infant with cachexia; rib shows thinner chondrocyte columns and disarray of the vasculature on "top" (hematoxylin-eosin, original magnifications ×4 [A and B]).*

Figure 4. *Adrenal stress changes. A, Acinar formation in definitive cortex with hemorrhage. Adrenal cortex with focal staining (B) and diffuse staining (C) consistent with severe chronic stress (hematoxylin-eosin, original magnification ×4 [A]; oil red O, original magnifications ×2.5 [B and C]).*

Table 5. Cerebellar Development and Maturation				
Layers	**16–20 wk**	**20–24 wk**	**24–28 wk**	**28–30 wk**
Outer granular[a]	Equal thickness	Equal thickness	Equal thickness	Equal thickness
Outer acellular[a]	Equal thickness	Equal thickness	Equal thickness	Equal thickness
Purkinje cells	Small pyknotic nuclei	Enlarged nuclei	Enlarged round cells	Display cytoplasm
Lamina dissecans	Develops	Distinctly present	Becomes narrow	Ablated
Inner granular	Scanty round cells	Occasional granular cells	More numerous granular cells	Sparsely cellular

[a] The outer granular and outer acellular layers are compared to each other in the corresponding columns throughout their 2 rows.

mark–shaped incision is made into the scalp from ear to ear and down the back to the nape of the neck. The scalp tissues are examined for cephalohematoma and localized edema. The soft tissues at the upper cervical column are resected to expose the foramen magnum, and the posterior segment of the atlas bone is cut away to expose the dura from where cerebrospinal fluid may be aspirated. When the body is prone with the occiput at the same level as the spine, the volume of fluid is a reflection of the reserve space within the cranium; diminished fluid is a marker of cerebral edema. After the dura is more widely opened, the level of the cerebellar tonsils is assessed. In older infants and children, the level represents a further index of raised intracranial pressure. At this juncture, Arnold-Chiari or Dandy-Walker malformation can be recognized. The very upper end of the spinal cord is removed for histologic analysis to evaluate for possible syringomyelia.

The right side of the calvarium is opened to the right side of the sagittal suture and sinus, and the frontal and parietal bones are reflected to the side of the head to expose the right cerebral hemisphere. This is then removed while keeping the falx and tentorium intact for in situ inspection.

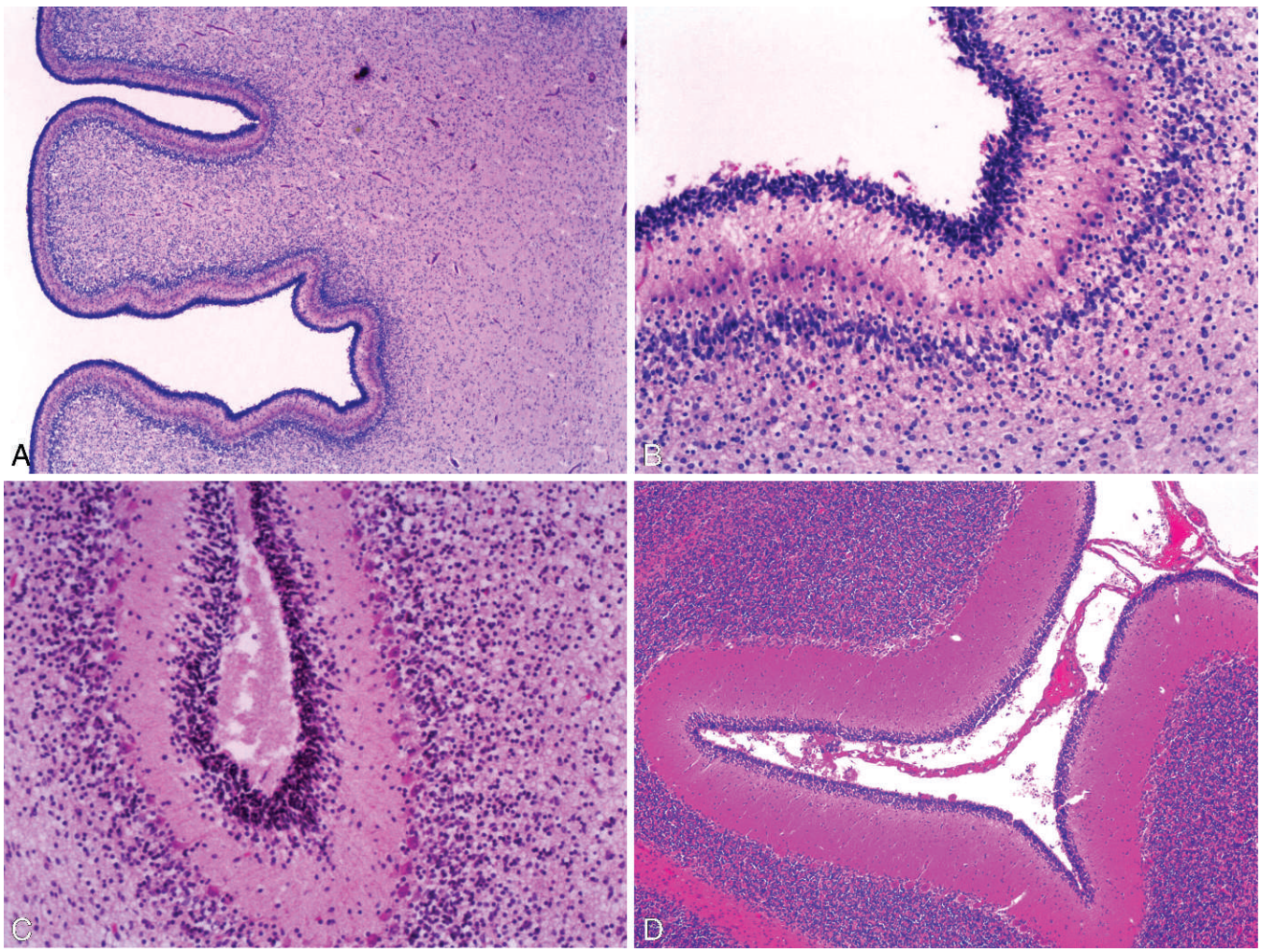


Figure 5. *Histologic profile of maturing cerebellum. Histologic appearance of cerebellar cortex at 27 to 28 weeks gestation, before Lamina dissicans is ablated (A and B), at 30 weeks gestation after Lamina dissicans is ablated (C) and at 2 months postnatal age (D) (hematoxylin-eosin, original magnifications; ×2[A]. ×10 [B and C] and ×4 [D].*

Table 5. Extended				
31–32 wk	**33–34 wk**	**35–36 wk**	**37–40 wk**	**6 mo**
Equal thickness	1/3 thickness	1/4 thickness	1/5 thickness	1–2 cells thick if still present
Equal thickness	2/3 thickness	3/4 thickness	4/5 thickness	Broad
Have nucleoli	Cytoplasmic processes appear	More processes	Mature appearance	Fully mature
Ablated	Ablated	Ablated	Ablated	Ablated
Increasing cellularity	Cellular with clumping	More clumping	Mature	Mature

Removal is achieved by dividing the corpus callosum, the cerebellar peduncles, the cranial nerves, and carotid vessels at the base of the skull. Thereafter, the falx is inspected and removed, followed by the left cerebral hemisphere, such that the whole tentorium is now exposed and can be inspected while intact for tears and hemorrhages. The hindbrain is then easily removed, followed by removal of the pituitary and inspection of the middle and inner ears by using strong bone cutters for access. Any sign of pus requires bacterial culture.

The spinal cord is appropriately removed in infants by laying the eviscerated body flat and using a sharp scalpel to cut through the cartilaginous junctions between vertebral arches and vertebral bodies. Cutting the vertebral bodies away, with the scalpel at an angle of a few degrees relative to the horizontal surface, the whole length of spinal cord can be exposed. The cord is removed by cutting through the nerve roots with the dura still intact. The dura should be opened longitudinally to facilitate formalin fixation.

When present, kernicterus is usually recognizable on the cut surfaces of the peduncles as deep yellow bile staining. A single mid-coronal cut through 1 hemisphere will also show bile staining in the basal ganglia. Should there be access to imaging facilities, a postmortem cerebral magnetic resonance imaging is quite sensitive in identifying central nervous system lesions. Provided appropriate consent is given, cerebrospinal fluid can be drained by cutting into the intact dura at the fontanelles while the brain is still in the skull and immersing the whole body in 15% to 20% formalin for a prolonged period. Alternatively, the unopened intact cranium can be dissected from the face and mandible and be fixed in 15% to 20% formal saline for a prolonged period. The fontanelles should be opened to facilitate diffusion of fixative into the subdural space. This method of removing the brain within its bony coverings is an adaptation of that described by Laurence and Martin[11] in 1959 whereby the posterior scalp is reflected from the calvarium as far as the ramus of the mandibles, the attachments of the pinnae are severed, and temporomandibular joints are disarticulated. The anterior scalp is reflected over the face to the supraorbital margins and the bridge of the nose. Skin is dissected from the nasal bridge and sides. The frontal sinuses or orbital septae are cut to expose periorbital fat and the eyes are expressed forward with a scalpel handle. The muscles and nerves are severed so that the eyes remain attached to the skin, which is further reflected forward. An oblique cut with a handsaw is then made through the bridge of the nose and zygoma to the pharynx. Remaining fascia and muscle are cut to remove the skull from the vertebral column at foramen magnum or the upper 2 cervical vertebrae, as may be preferred, depending upon the anticipated intracranial pathology. Reconstruction of the head is achieved by using sawdust in moist lint with cotton wool and plaster of Paris.

Whichever method is used for removing the brain from the skull in fetuses and young infants, the configuration of the gyral and sulcal patterns of development of the cerebral hemispheres should be compared with published diagrams that indicate increasing complexity with advancing gestational age, as this is a relatively reliable tool for determining gestational age in preterm neonatal deaths.[12–14]

RECORDING MACROSCOPIC FINDINGS

Given that child abuse and neglect are relatively prevalent in Africa, a pathologist may begin to perform a routine teaching autopsy and discover, during the dissection process or later when assimilating ancillary test results, that there are medicolegal implications. It is therefore prudent to develop a habit of making accurate and detailed recordings of the findings where statements such as "No abnormality discovered" are avoided.

Although often criticized for being either too incomplete or excessively detailed, the use of formulated templates tailored to stillbirths and very young infants is most helpful in recording the autopsy findings. When reporting autopsies on older children and in cases that are candidates for possible inquest or professional negligence, there is value to recording the findings as the dissection proceeds. Here the disadvantage is that positive findings are often not described in a systematic order for easy evaluation by second parties.

Table 6. Histologic Assessment of Maturation in Cerebellum and Periventricular Germinal Matrix

Between 16 to 28 weeks' gestation, the cortex of the cerebellum has 5 layers consisting of inner and outer granular layers and an additional central granular layer (lamina dissecans) containing immature Purkinje cells that begin to enlarge at about 24 to 28 weeks and have distinctive nucleoli at about 30 to 32 weeks. The outer granular layer is as thick as the immediately underlying nongranular layer until about 32 weeks. Thereafter, it progressively gets absorbed to disappear altogether at 5 to 7 months' postnatal age. In addition, the nongranular layer between the inner granular layer and the central lamina dissecans is progressively ablated and finally absorbed into a thickening inner granular layer at about 28 to 30 weeks.[9–11] The ratio of outer granular layer to outer nongranular layer changes from 1 to 1 at 30 to 32 weeks to 1 to 2 at 33 to 34 weeks to 1 to 3 at 35 to 36 weeks and to 1 to 4 at 37 to 38 weeks. These sequential changes are illustrated in Figure 5. The neuronal and glial cells of the cerebral cortex develop from cells that migrate from periventricular germinal matrix closely adjacent to the lateral ventricles. This migration should normally be complete between 35 and 36 weeks at the inferior horns and by 40 weeks at the anterior aspect under corpus callosum.[9] Continued retention of immature matrix cells adjacent to the ventricles or manifesting as clusters arrested in migration is an index of delayed intrauterine development.

Table 7. Histologic Assessment of Maturation of Kidneys
Glomerulogenesis begins in the metanephros at about 14 to 16 weeks' gestation as a result of stimulation from the penetrating ureteric bud so that a multilobulated primitive kidney forms. It has about 8 lobules at 20 weeks and 35 to 40 at 40 weeks. It undergoes a period of rapid growth and development between 23 and 32 or 33 weeks of gestation when a new layer of glomeruli forms each week. The layers may be counted in appropriately orientated histologic sections between adjoining columns of Bertin. At 23 weeks there are 3 layers, and 1 layer is added each week for the next 10 or 11 weeks.[9,13] The recognition of glomerulogenic layers to be counted is illustrated in Figure 6. Thereafter, additional glomeruli are added to the outer subcapsular layer until 36 weeks' gestation when glomerulogenesis ceases and there should be 12 to 14 layers. Appropriate orientation is achieved by selecting tissue sections that are cut perpendicularly to the intact renal capsule. Such sections should display longitudinally cut collecting tubules in the medulla. These estimates of gestation are considered to be within 1 week or 2 of actual gestation but do not apply in certain chromosomal anomalies such as Down syndrome as well as in abnormalities of renal development such as Potter sequence and in dysplastic kidneys.

In addition, forensic cases require a distinctive preamble that varies slightly from country to country but where the pathologist always indicates his/her qualifications and experience. The preamble usually includes the date, time, and place of the autopsy; the names and qualifications of other persons in the mortuary at the time that the autopsy is being performed; how the body is identified; who has given consent or ordered the autopsy; how this has been obtained; and what restrictions apply. In all cases, body weight and external measures, as indicated in Table 1, should be undertaken and be compared with expected norms for gestational or postnatal age or body length. Such tables are available in textbooks of pediatric pathology.[1–6,15,16] The recently formulated tables prepared by Maroun and Graem[15] are highly recommended but Stocker and Dehner[6] provide a wider spectrum of normative values.

Appropriate photographs should be taken of frontal, posterior, and side views of the whole body as well as of the face and hands.

A suggested template for dealing with early fetuses and stillbirths is shown in Table 2. This is easily adaptable for older children and for inquest cases. The names of the mortician assisting with the autopsy and of any other witnesses, as well as the means by which the body is identified, should be recorded for possible unanticipated future medicolegal processes. Weights and measures are usually recorded in a table format that includes the expected norms. Individual organ weights may also be listed with the macroscopic description of each organ.

It is good practice to provide the autopsy-requesting officer with a detailed provisional report that indicates the tentative cause of death so that accurate death certificates may be issued and information can be conveyed to the family of the deceased.

POSTMORTEM HISTOLOGY

Microscopic examination of tissues serves 3 different purposes: making an assessment of developmental maturation during intrauterine and postpartum life, evaluating possible adverse processes that occur during the period that immediately precedes death, and confirming or determining the pathologic process that led to death. Evaluating the duration of illness or other pathologic processes helps to determine both the mechanisms of disease and their sequence preceding death. In this respect, routine sampling of the following tissues should be regularly undertaken:

Larynx, demonstrating a cross section of the vocal cord and its surface epithelium to evaluate for ulceration, edema, hemorrhage, and inflammation (Figure 1, A through C);

Thymus to evaluate for small hemorrhages, a stress reaction, and involutionary changes (Table 3; Figure 2, A through C);

Rib costochondral junction to assess the duration of terminal stress and possible underlying rickets and/or scurvy (Table 4; Figure 3, A and B);

Adrenal glands to evaluate for cortical lipid content, pseudoacinus formations, necrosis, hemorrhages, and retention of fetal cortex (Figure 4, A through C);

Cerebellum and the paraventricular area of the brain below the corpus callosum (Tables 5 and 6; Figure 5, A through D);

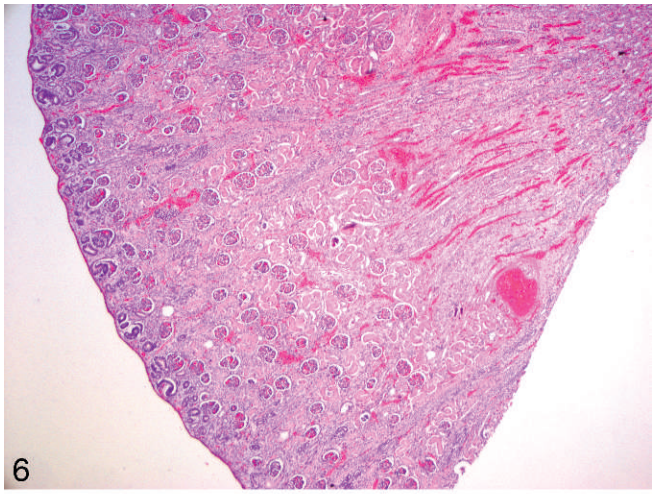
Kidney sectioned at right angles to capsule to count glomerular generation (Table 7; Figure 6);

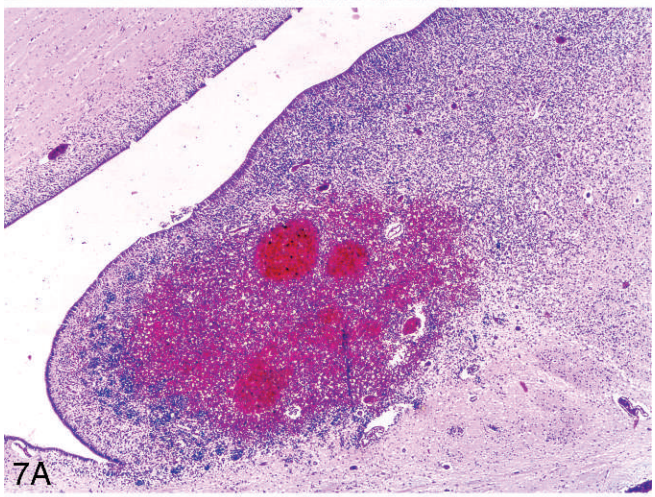
Lungs sampled midway between the hilum and the most distant periphery of each lobe to discern whether or not patchy pathologic findings are sufficient to explain death.

The undertaking of a thorough pediatric autopsy will always require the routine sampling of many tissue portions that add to labor and costs. A comprehensive list is given in Table 8; ideally, tissues should be sampled, processed into paraffin-embedded blocks, cut, and stained. Where resources are very limited, a selection of the tissue portions may be made for cutting, staining, and initial reporting. Paraffin blocks may comprise several small samples from multiple tissues. The choice should be made upon the basis of provided clinical data and gross autopsy findings with the knowledge that some of the otherwise unobtrusive lesions will be missed.

DEVELOPMENTAL MATURATION

Developmental maturity and organ function will usually match gestational and chronologic age but this is not always the case. Impaired maturation of particular organs may be due to an inherent genetic or chromosomal abnormality or to a gestational disorder or illness of either the mother or fetus. Particular organs more easily lend themselves to assessment for developmental impairments. Changes in the microanatomy of the cerebellar cortex (Tables 5 and 6; Figure 5), the regression of germinal matrix in the paraventricular areas of the brain, the formulation of glomeruli in the kidneys, and the development of pulmonary acini are parameters that are useful in assessing developmental maturity. These processes are well described in standard textbooks of pediatric and fetal pathology. It should, however, be noted that all organs and tissues do not always mature synchronously and that formulated stages are part of a widely based Gaussian curve. The sequential developmental changes that occur in the cerebellum and paraventricular tissues, as adapted from Larroche[13] (1977) and





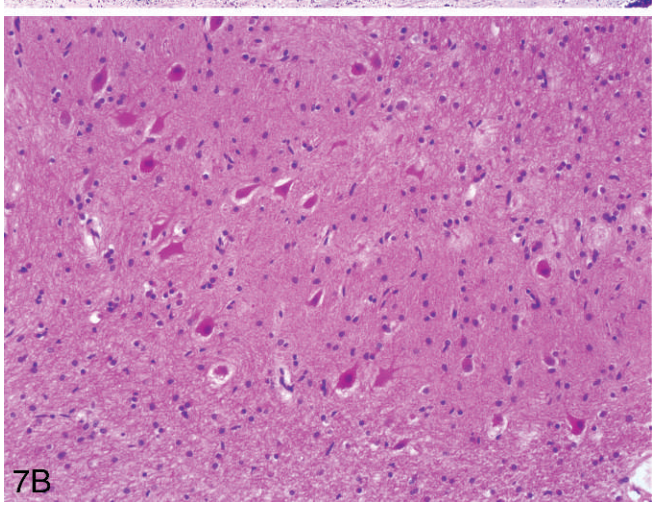


Figure 6. *Renal maturation. Twnety-nine weeks' gestational age fetal renal cortex (hematoxylin-eosin, original magnification ×4).*

Figure 7. *Hypoxic changes in central nervous system. A, Germinal matrix bleed in premature infant. B, Hypoxic changes of dentate nucleus: prominent neuron necrosis and gliosis (hematoxylin-eosin, original magnifications ×1 [A] and ×20 [B]).*

Rakic and Sidman[14] (1970), and as reported by Dorovini-Zis and Dolman[12] in 1977 recorded for the kidneys by Singer et al[16] in 1991, are described and illustrated in Tables 6 and 7, and Figures 5 and 6.

Table 8. Tissue Selection for Processing to Paraffin Blocks

Brain (frontal and occipital cortex, lateral corpus callosum with caudate nucleus, Ammon horn or hippocampus with adjoining temporal lobe cortex and paraventricular tissue, pons with acqueduct, midbrain medulla and cerebellar cortex with dentate nucleus).
Spinal cord (cervical, thoracic, and lumbar).
Lungs (each lobe midway between hilum and periphery).
Heart (atrioventricular junction for each side that includes full-thickness myocardium with atrioventricular valve cusps and papillary muscle of ventricles as well as upper atrial and ventricular septum to show conducting system).
Larynx with vocal cord cut transversely.
Trachea with attached thyroid cut transversely.
Longitudinal sections of gastroesophageal and gastroduodenal junction.
Transverse sections of duodenum at ampulla of Vater with attached head of pancreas, jejunum, ileum, colon, and appendix.
Kidneys cut perpendicularly to external surface to show straight collecting tubules.
Adrenals cut sagittally.
Left and right lobes of liver with gallbladder.
The costochondral junction of a fifth rib end cut longitudinally to also include bone marrow.
Thoracic and mesenteric nodes whereby the thoracic node includes an adjacent main bronchus.
Thymus, pituitary, salivary gland, tonsil, tongue, spleen, tail of pancreas, a gonad, urinary bladder, psoas muscle, aorta, and any lesion that may be encountered with adjoining host tissue in skin, uterus, prostate, urethra, ureter, and anus.

STRESS REACTIONS

Assessing the duration of preceding stress and or illness is achieved by microscopic examination of particular organs. The *thymus* is considered to be most helpful when survival, after the onset of the stressful event, has been longer than 12 to 18 hours. Figure 2 illustrates stages of thymic stress reaction and Table 3 indicates the sequence of changes that occur during a terminal illness, where "macrophages" refer to the "starry sky" appearance of the cortex reported by Emery[17] in 1964 and "mulberries" refer to small clusters of lymphocytes. In addition, as the fifth rib is considered to be the most rapidly growing bone during late pregnancy and infancy, microscopic examination of its *costochondral junction* is useful.[18] Here, alterations in growth are readily detected but the duration of preceding illness is influenced by the duration of gestation or postnatal age and any underlying subclinical rickets or scurvy. The sequence of changes and the interpretation of their duration, shown in Table 4, are adapted from the formulation of Emery, Sinclair-Smith and coworkers from 1964 to 1976[17–19]. Figure 3, A, illustrates normal rib-end growth with straight single file columns of activated chondrocytes in direct contact with capillaries. Figure 3, B, illustrates short-term impaired rib-end bone growth with early clustering of activated chondrocytes separated from blood vessels by intervening cartilaginous matrix, as enunciated by Sinclair-Smith et al[19] (1976).

During a state of shock the *adrenal glands* will convert their lipid reserves into corticosteroid hormones. This can be recognized macroscopically as loss of the deep yellow coloration of the definitive cortex and histologically by clearing of the cortical cells. This phenomenon can be confirmed with oil red O staining for neutral fat (Figure 4). In addition, the subcapsular adrenal cortex often assumes a pseudoacinar configuration with small hemorrhages in

stressed stillbirths. This observation first reported by De Sa[20] also occurs postnatally after intense, short-duration stress (Figure 4, C).

CEREBRAL HYPOXIA AND ISCHEMIA

Cerebral hypoxia and ischemia have a significant role in explaining the mechanism of death in the very young. This is often because of the prevalence of various forms of placental pathologic processes,[21] frequent respiratory infections, and congestive cardiac failure at this time of life. As a consequence of ischemia or hypoxia, hemorrhages most often occur in the germinal matrix of the ventricles (Figure 7, A), cerebellum, and around small blood vessels (ring hemorrhages). Parenthetically, it is remarkable how much brain tissue can become infarcted and still permit relatively normal growth and development, whereby clinical milestones may only be minimally delayed. Neuronal changes consist of nuclear pyknosis and enhanced cytoplasmic eosinophilia, which are most readily seen in the dentate nucleus of the cerebellum (Figure 7, B), the Purkinje cells, Ammons horn of the hippocampus, and the nuclei of the pons and midbrain. The classical changes may appear only when there has been survival after the hypoxic event for more than 18 to 36 hours, although similar changes are sometimes seen after a much shorter interval.

Congestion of the small white matter vessels helps to distinguish pure hypoxia from ischemia.

Periventricular leukomalacia is a form of coagulative necrosis associated with tissue lysis, edema, cyst formation, and gliosis and signifies an intrauterine ischemic event most commonly manifest in prematurity.

CONCLUSION

When all the sampled tissues have been examined and the results of ancillary tests are available, a final anatomic diagnosis is issued. An opinion should be expressed on the relevance of positive and negative bacteriology and virology culture findings in the light of the particular postmortem interval.[22] The final diagnosis should list all the anatomic and ancillary abnormalities that contributed to the death of the patient in order of their importance. In addition, the pathologist should provide an interpretation of the sequence of events leading to death. It is important to ensure that all questions raised by the requesting parties have been addressed. There are occasions when the pathologist should recommend that particular corrective action be taken to avoid recurrences of harmful events, such as vitamin A and drug overdosage and excessive exposure to Mercurochrome (Resmed, Durban, South Africa) on skin wounds and omphaloceles. The final report should indicate the number of paraffin blocks that have been processed and their organ of origin. It should be dated on the day of issue.

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