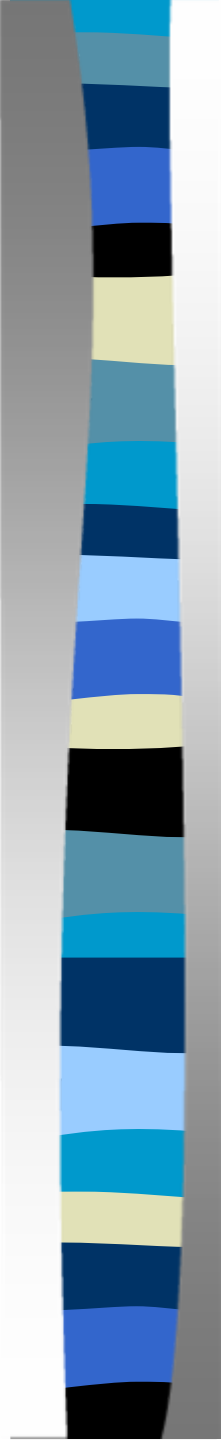
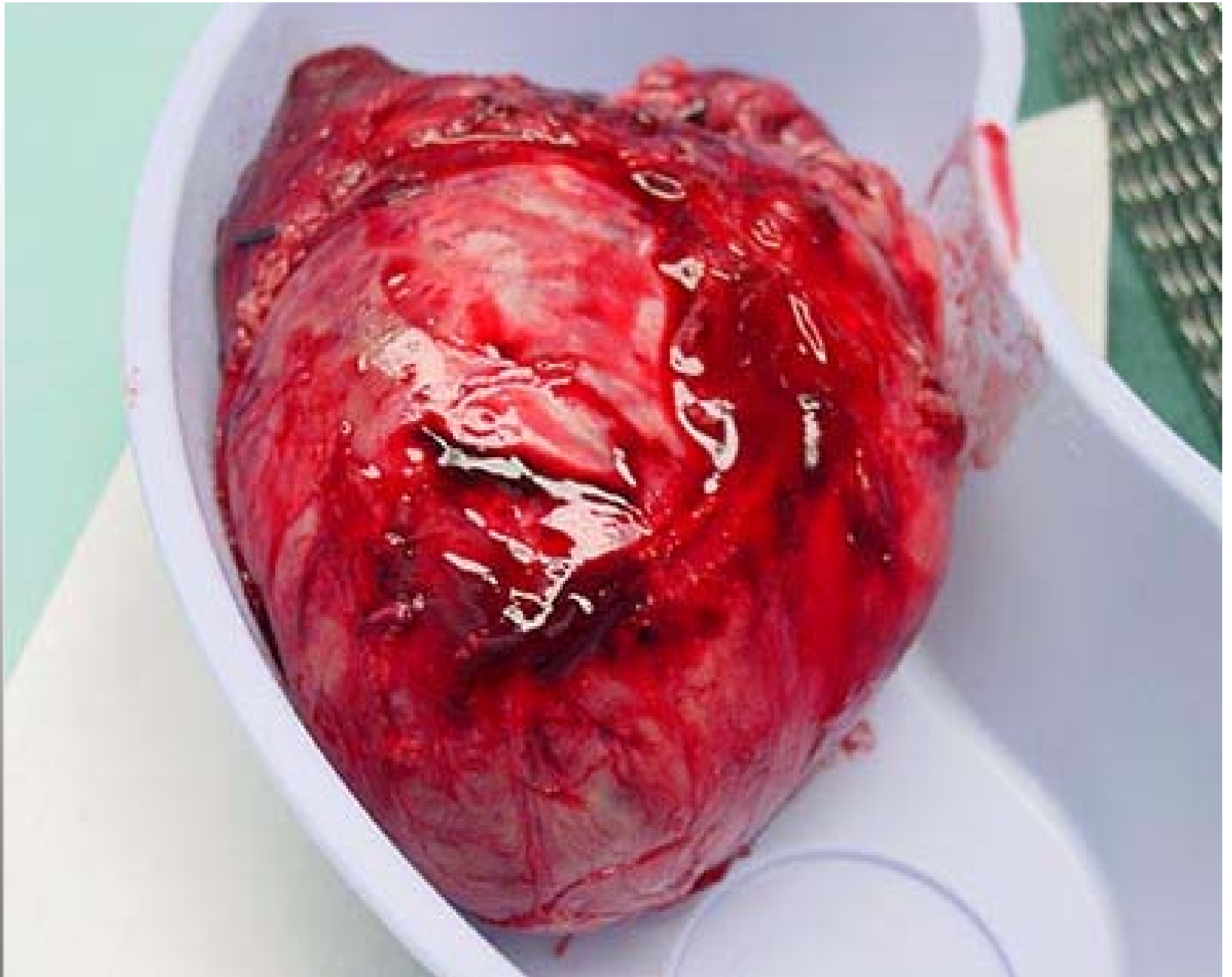


Adrenocortical Cancer

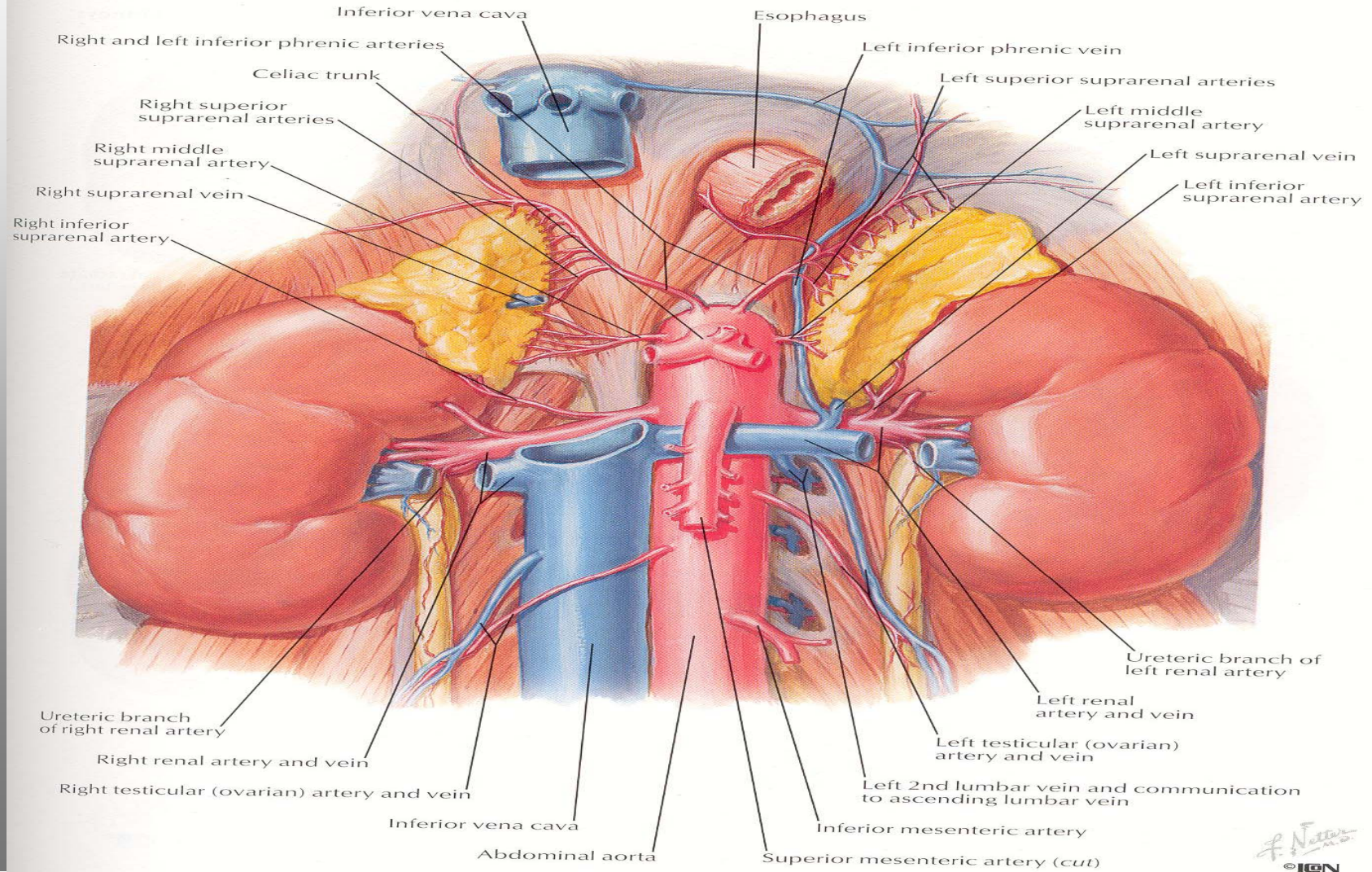
A decorative horizontal bar consisting of a series of colored segments in shades of blue, teal, yellow, and black, arranged in a slightly wavy pattern across the width of the slide.

In a Child





Anatomy of Kidneys, Adrenal Glands





Abdominal Masses in Children

■ Neuroblastoma

- the most common abdominal malignancy
- 1 case per 10,000 persons
- of neural crest origin (may arise anywhere throughout the sympathetic ganglia or adrenal medulla)
- median age at diagnosis is 2 years old
- Only about 25% present with a solitary mass curable with surgery; most present with extensive locoregional or metastatic disease that has an overall survival of less than 30%



Abdominal Masses in Children

- Presenting symptoms
 - Depends on site and metabolic activity
 - Most commonly, a fixed lobular mass extending from the flank toward the midline
 - abdominal pain, distention, weight loss, anorexia, or bladder / bowel dysfunction may be noted
 - stridor or dysphagia
 - Horner's syndrome: ptosis, anhidrosis, miosis
 - Involuntary movements, diarrhea (from secretion of VIP), hypertension
 - Metastasis usually occurs to cortical bones, bone marrow, and liver



Abdominal Masses in Children

- Definitive diagnosis is by histologic evaluation of tissue
 - high urine catecholamine metabolites (homovanillic and vanillylmandelic acid) are highly suggestive
- CT and MRI are preferred for radiographic examination
- Complete staging includes
 - CT scan of chest, bone scan, bone marrow aspirate and biopsy
- Therapy is multimodal including surgery, chemotherapy, radiation, and immunotherapy
 - Children with localized disease and infants have the best survival while older children with advanced-stage disease have a poor prognosis even with intensive therapy



Abdominal Masses in Children

■ Wilms' Tumor

- embryonal tumor of renal origin
- the most common primary malignancy of the kidney in childhood
- peak incidence is between 3 and 4 years of age
- bilateral disease is present in approximately 13% of cases
- hereditary disease is uncommon, although many germline mutations have been identified in many genes including WT1 on chromosome 11
- associated abnormalities include aniridia, cryptorchidism, hypospadias, Beckwith-Wiedemann syndrome, Denys-Drash syndrome, and WAGR syndrome



Abdominal Masses in Children

- Presenting symptoms
 - often asymptomatic except for palpable abdominal mass
 - hypertension
 - hematuria
- Definitive diagnosis is by histologic evaluation of tissue
- US is the initial imaging modality
 - CT or MRI may be necessary to differentiate Wilms' and neuroblastoma (as well as urinary catecholamines)
- Complete staging includes
 - CT and MRI of abdomen and pelvis, CT scan of chest
- Therapy is multimodal depending on the stage and includes surgery, radiation therapy, and chemotherapy
 - current overall survival exceeds 85%



Abdominal Masses in Children

■ Others

- Rhabdomyosarcoma, hepatoblastoma or hepatocellular carcinoma, and teratoma



Adrenal Glands

■ Adrenal medulla

- derived from ectoderm and is an extension of the sympathetic nervous system
- releases catecholamines
- norepinephrine is converted to epinephrine in the medulla
- Pheochromocytoma
 - rare, catecholamine-producing tumor usually found in the adrenal medulla, although it can occur in any sympathetic ganglion
 - are usually benign (90%), unilateral (90%), and sporadic
 - 10 to 20% occur in the context of a genetic syndrome - von Hippel-Lindau disease, multiple endocrine neoplasia type 2, and neurofibromatosis being the most common



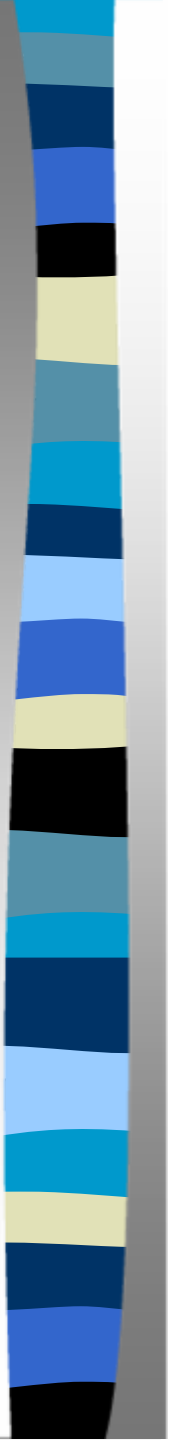
Adrenal Glands

- Symptoms and Signs of Pheochromocytoma
 - paroxysmal headache, tachycardia, and diaphoresis
 - hypertension
 - Elevation of urinary catecholamine excretion (measuring epinephrine, norepinephrine, metanephrine, or homovanillic acid in a 24-hour collection) is highly specific for disease
- CT and MRI are indicated for imaging
 - Metaiodobenzyl guanidine (MIBG) scanning is specific for pheochromocytoma, but is most useful for determining the extent of metastasis in malignant pheochromocytoma or for localizing nonadrenal tumors
- Treatment includes surgical extirpation after alpha- and beta-adrenergic blockade

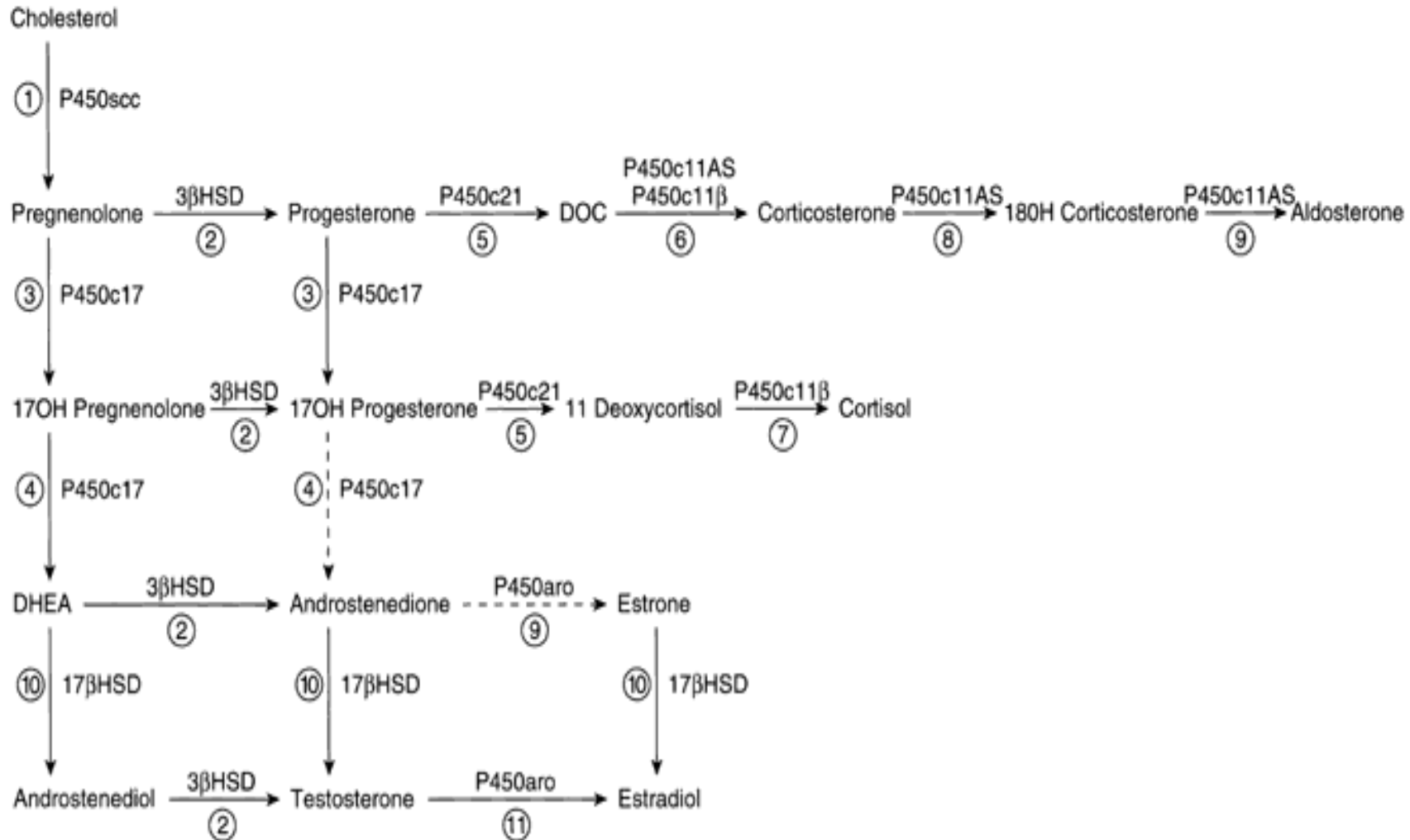
Adrenal Glands

■ Adrenal cortex

- derived from mesoderm
- produces mineralocorticoids (principally aldosterone), glucocorticoids (principally cortisol), and adrenal androgens
- the fetal adrenal cortex has two zones (the adult cortex is divided into the glomerulosa, fasciculata, and reticularis)
 - an outer definitive zone, which is the principal site of glucocorticoid and mineralocorticoid synthesis
 - an inner fetal zone, which makes androgenic precursors for the placental synthesis of estriol



Principal pathways of human adrenal steroid hormone synthesis





Congenital Adrenal Hyperplasia

- Any one of many disorders involving a genetic lesion in one of the steroidogenic enzymes interfering with normal steroidogenesis
- The signs and symptoms of the disease are caused by deficiency of the steroidal end product and the effects of accumulated steroidal precursors proximal to the blocked step
- Deficiency of 21-hydroxylase accounts for approximately 95% of the genetic disorders of steroidogenesis
 - results in glucocorticoid and mineralocorticoid deficiency and testosterone excess which may cause ambiguous genitalia at birth



Adrenal Insufficiency

- Adrenal insufficiency can be caused by hypopituitarism and ACTH deficiency, or it can be caused by a primary adrenal disorder.
- Causes of adrenal insufficiency
 - Autoimmune
 - Tuberculosis, fungal infection
 - Sepsis
 - AIDS
 - Congenital adrenal hyperplasia
 - Adrenal hemorrhage or infarction
 - Congenital adrenal hypoplasia
 - Unresponsiveness to ACTH
 - Withdrawal from glucocorticoid therapy
 - Hypopituitarism
 - Hypothalamic tumors



Adrenal Insufficiency

- Symptoms/Signs of adrenal insufficiency

- Anorexia
- Apathy and confusion
- Dehydration
- Fatigue
- Hyperkalemia
- Hypoglycemia
- Hyponatremia
- Hypovolemia and tachycardia
- Nausea and vomiting
- Postural hypotension
- Salt craving
- Weakness
- Sparse pubic and axillary hair
- Diarrhea
- Hyperpigmentation
- Weight loss



Adrenal Excess

- Aside from the congenital adrenal hyperplasia, causes of excess adrenal steroid production are rare, falling into three categories—glucocorticoid excess (Cushing syndrome), mineralocorticoid excess (Conn syndrome), and virilizing and feminizing adrenal tumors.
- Cushing syndrome
 - often is used to describe any form of glucocorticoid excess
 - Cushing disease is hypercortisolism caused by pituitary overproduction of ACTH
 - Among adults and children older than 7 years, the most common cause of Cushing syndrome is true Cushing disease
 - Among infants and children younger than 7 years, adrenal tumors predominate.



Adrenal Excess

– Signs and symptoms of Cushing's syndrome

- Weight gain
- Poor growth
- Fatigue
- Delayed puberty
- Bruising
- Headache
- Nocturia
- Osteopenia
- Hypertension
- Plethora
- Acne
- Hirsutism
- Striae
- Buffalo hump
- Delayed bone age



Adrenal Excess

- Lab tests to evaluate Cushing syndrome / disease
 - serum cortisol
 - diurnal variation
 - serum ACTH
 - low and high dose dexamethasone suppression tests

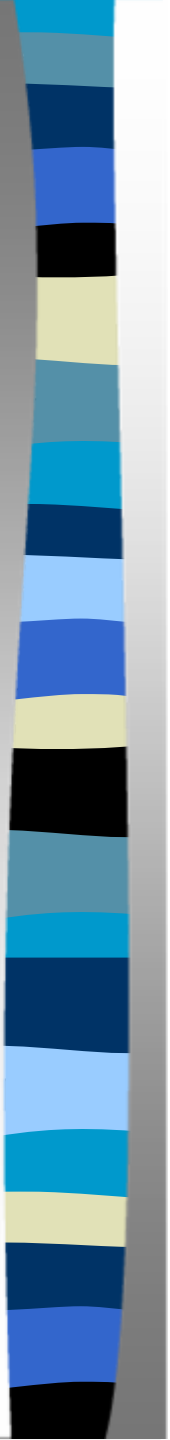


Adrenal Excess

- Ectopic ACTH syndrome
 - Although it is rare among children, ectopic ACTH syndrome has been found among infants younger than 1 year.
 - Associated tumors have included neuroblastoma, pheochromocytoma, and islet cell carcinoma of the pancreas.
- Conn syndrome
 - rare among children
 - characterized by hypertension, polyuria, hypokalemic alkalosis, and low plasma renin activity caused by aldosterone-producing adrenal adenoma

Adrenal Excess

- Virilizing / Feminizing Adrenal Tumors
 - Most are adrenal carcinomas that produces a mixed array of androgens and glucocorticoids





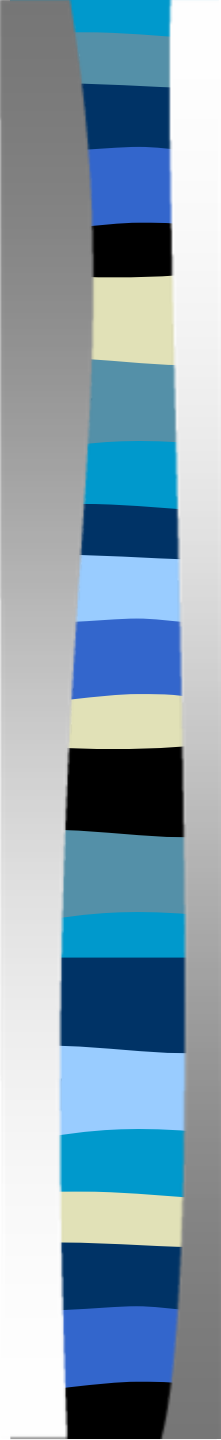
Adrenocortical Tumors

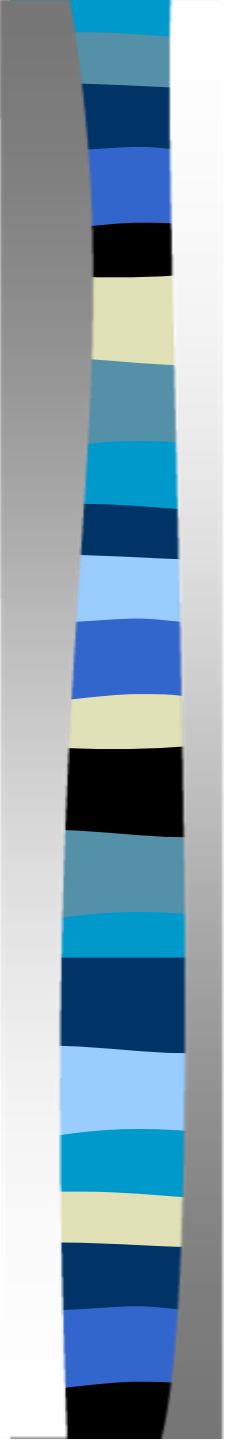
- Rare in children and adolescents
 - 14 new cases per year in individuals less than 20 years of age in the US
 - Two major types:
 - adrenal adenomas
 - benign neoplasms that can be functionally autonomous
 - hypercortisolism and hyperaldosteronism are common but seldom virilization or feminization



Adrenocortical Tumors

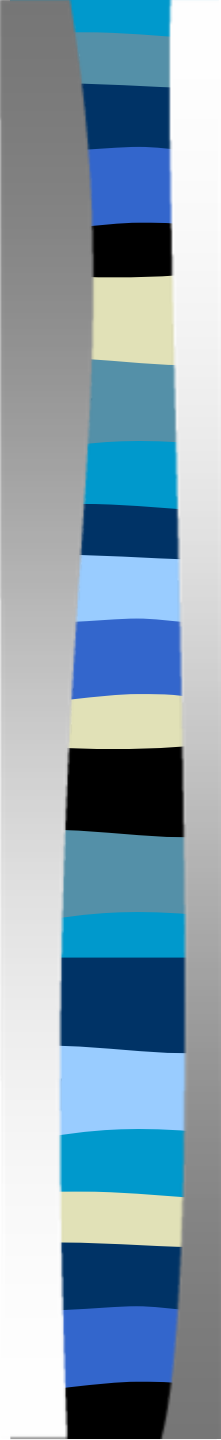
- Adrenocortical carcinoma
 - median age 3.2 years
 - female predominance in most age groups
 - 90% of children have clinical evidence of an endocrine syndrome
 - most cases appear sporadic, although several hereditary cancer syndromes include this cancer
 - » Li-Fraumeni syndrome (p53 tumor suppressor), Beckwith-Wiedemann syndrome (chromosome 11), MEN type 1 (chromosome 11)

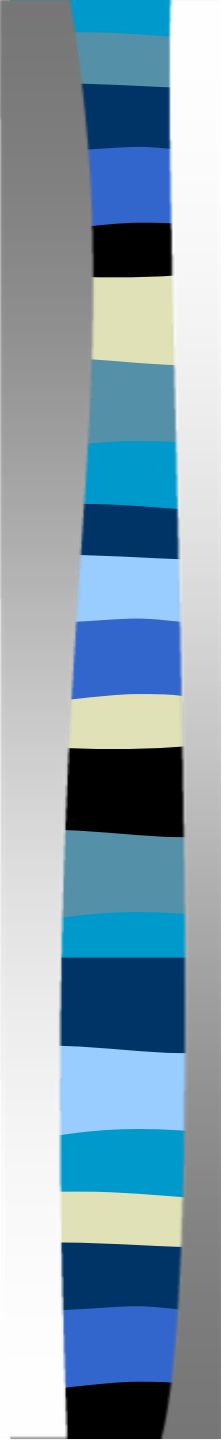
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- Clinical presentation of adrenocortical carcinomas
 - 90% of children have clinical evidence of an endocrine syndrome
 - virilization, alone or in combination with overproduction of other adrenal hormones, is the most common clinical presentation
 - Diagnostic evaluation
 - pheochromocytoma, hyperaldosteronism, hyperandrogenism, and Cushing's syndrome should be ruled out by history/physical and laboratory tests
 - US, CT, and MRI are indicated
 - » CT can usually distinguish adenomas from carcinomas
 - » MRI more readily identifies local invasion and involvement of the vena cava
 - Metastasis are most common in the liver, lungs, lymph nodes, and bone
 - » As such, CT chest and bone scan indicated

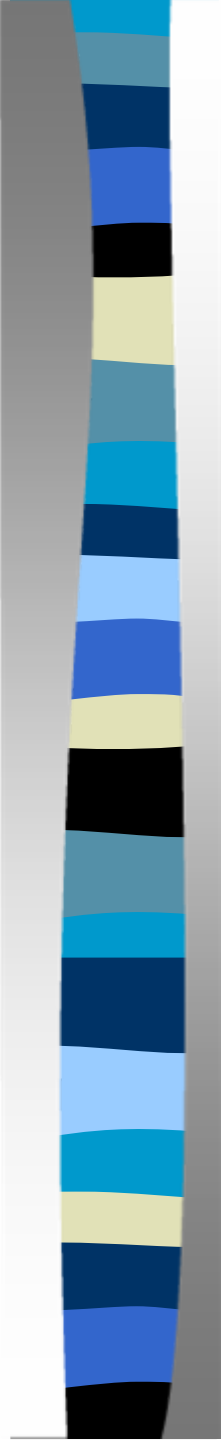
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- Tissue biopsy confirms the disease, although it may be difficult to differentiate adenoma from carcinoma histologically

- Treatment

- excisional biopsy should be performed of all adrenocortical tumors, as surgical resection is the only potential cure
- solitary recurrences or metastases should be removed surgically
- If resection is not surgically possible, chemotherapy with mitotane is usually initiated with the hopes of tumor regression to resectability
 - » Mean survival does not appear to be changed with chemotherapy
 - » side effects include: nausea, vomiting, diarrhea, somnolence, weakness, dizziness

- 
- Prognosis is generally poor
 - Localized disease has a better prognosis with age younger than 3, virilization alone, normal blood pressure, absence of tumor spillage during surgery, and tumor weight less than 200g
 - Advanced disease has a dismal outcome
 - mean survival approximately 18 months

- 
- Michalkiewicz, E., et al: Clinical and Outcome Characteristics of Children With Adrenocortical Tumors: A Report From the International Pediatric Adrenocortical Tumor Registry. *Journal of Clinical Oncology* 22:838-845, 2004.
 - Descriptive analysis of 254 patients younger than 20 with newly diagnosed or previously treated adrenocortical tumors from Jan. 1990 - Dec. 2001
 - Central review of tumor histology was not a requirement for registry
 - Patients with a diagnosis of either adenoma or carcinoma histologically were included in the study
 - No central review of imaging studies
 - Extent of disease was defined retrospectively as localized or advanced
 - Localized
 - Stage 1 - tumor completely excised with negative margins, tumor weight less than 200g, and absence of metastasis
 - Stage 2 - tumor completely excised with negative margins, tumor weight greater than 200g, and absence of metastasis
 - Advanced
 - Stage 3 - Presence of microscopic or gross tumor after surgical resection or inoperable tumor
 - Stage 4 - Hematogenous metastasis at presentation

- 
- Clinically, tumors were classified as functional or nonfunctional
 - Treatment of those in the study was done by the primary physician with consultation from a physician involved with the study
 - Surgery alone was recommended for localized disease
 - Patients with advanced disease received a variety of chemotherapy regimens
 - Patients with recurrent disease received attempted complete resection followed by chemotherapy

■ Flaws in the study

- Multiple variables in all aspects from diagnoses to treatment
- Limited number of patients with advanced stage disease
- Majority of patients from Southern Brazil, where adrenocortical tumors have a much higher incidence and different pathology