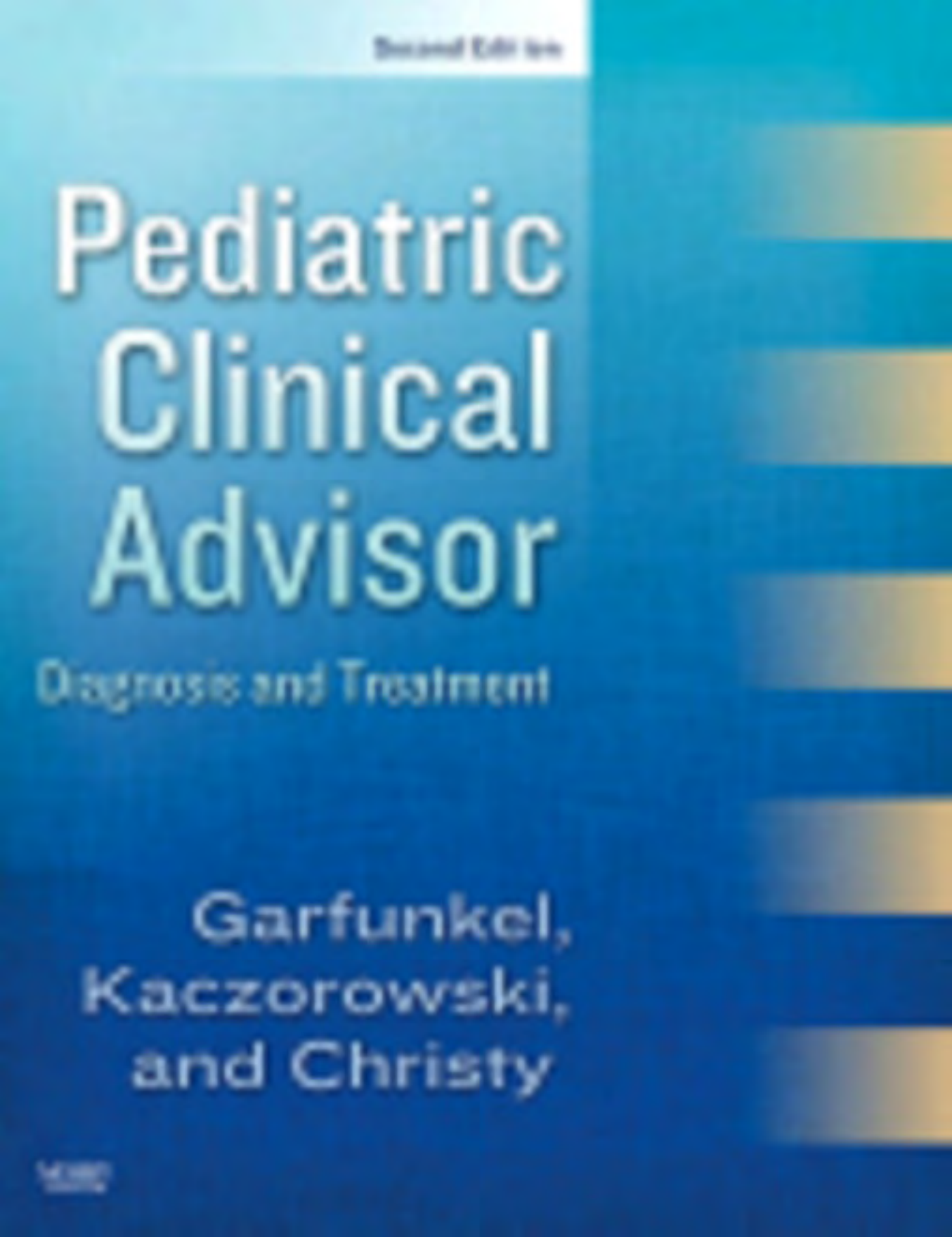
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To our spouses
Craig Orlowski,
Laura Jean Shipley, and
Ralph Manchester

To our children
Zachary and Rachel Orlowski,
Daniel Shipley, Emma and Jack Kaczorowski,
Eric, Alison, and Ian Manchester

And to our
Parents, mentors, colleagues, students, and friends,
who have encouraged and inspired us

Thank you all,
LCG, JK, CC

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Preface to the Second Edition

In this second edition of the *Pediatric Clinical Advisor,* the ready reference for busy pediatric clinicians, we reordered the major sections at the urging of our publishers. We have also added many new chapters at the advice and suggestions of our residents, students, and colleagues who realized that there were important missing topics in the first edition.

This "five-books-in-one" format includes updated or new information in each section. **Section I, Diseases and Disorders** covers nearly 400 clinical topics in easy to read bulleted format; **Section II, Differential Diagnosis** encompasses some 50 common differentials in table format; **Section III, Clinical Algorithms** leads the busy practitioner through diagnoses of more than 40 common signs and symptoms; **Section IV, Charts, Formulas, Tables, and Tests,** provides readers with those frequently used, difficult to locate when needed, tables, graphs, equations and charts. This section is organized by broad topic area to include: dermatology, development, emergency medicine (burns and concussion), equations and nomograms, growth charts, neurology, sports medicine and orthopedics (maneuvers, diagrams and conditions for participation), as well as selected vital sign charts and laboratory tests and interpretations. The new **Section V, Prevention** would seem to be amiss in a "rapid diagnosis" textbook; however, for most pediatricians and pediatric practitioners, primary and secondary prevention is part of every patient encounter. Whether it be an office visit for a child with asthma or otitis media with a parent who smokes; a well child check with an internationally adopted 2 year old, an 8 year old in foster care, or a sexually active teen; or an infant hospitalized with dehydration whose mother is depressed—prevention plays a key role in treatment. We have not only included routine immunization schedules and websites, but immunization and infectious disease prevention for travel and chronic diseases; nutrition guidelines and formula content; adolescent screening and birth control; smoking cessation assistance; risks and screening needs of internationally adopted children, children of incarcerated parents, and children in foster care; and screening and referral information for parental depression, divorce, and domestic violence.

We would like to take this opportunity to thank our many contributors and in particular would like to acknowledge Jean Brockmann for her steadfast dedication to the completion of this project.

Preface to the First Edition

You are between patients; the waiting room is full; and you are falling further behind. You need to review a clinical topic, broaden your differential diagnosis, initiate a diagnostic workup, or remember the latest treatment of a less common disease—this is what we had in mind when we created *Mosby's Pediatric Clinical Advisor*.

This textbook is meant to be a user-friendly, ready reference for the primary care physician, nurse practitioner, physician assistant, resident, or student. It is organized to lead you from signs and symptoms to comprehensive information about specific diseases and clinical problems, with supporting diagrams, tables, and formulas.

Part I presents differential diagnoses of more than 40 common signs and symptoms paired with diagnostic algorithms. **Part II** covers more than 350 clinical topics in a bulleted format including ICD-9CM codes, etiology, epidemiology and demographics, differential diagnosis, diagnostic workup, and therapeutic plans; it also contains pertinent websites and references. **Part III** includes those frequently sought graphs, equations, and charts that you can never seem to get your hands on, such as endocarditis prophylaxis, developmental screening tools, and the body mass index calculation with normative tables.

We wish to express our deepest appreciation to Jean Brockmann, our coordinator, who has worked kindly and tirelessly to facilitate and organize the production of this book. Thanks, Jean.

LCG, JK, CC

BASIC INFORMATION

DEFINITION

Acetaminophen (*N*-acetyl-*p*-aminophenol) is widely available as a single agent for relief of fever and pain. It is also widely available in combination cold and pain preparations. Acute and chronic types of over-ingestion are associated with gastrointestinal disturbance and potentially with fatal hepatotoxicity.

SYNONYMS

Acephen
APAP
Aspirin-free Anacin
Cetafen
Feverall
Genapap
Genebs
Infantaire
Liquiprin
Mapap
Medpap
Panadol
Paracetamol
Redutemp
Silapap
Tempra
Tylenol
Valorin

ICD-9-CM CODE
965.4 Acetaminophen poisoning

EPIDEMIOLOGY & DEMOGRAPHICS

- Acetaminophen is the most common potentially toxic ingestion in children younger than 6 years.
- In 2003, there were almost 40,000 acetaminophen exposures in children 0 to 6 years old.
  - Less than 2% of fatalities from acetaminophen toxicity occur in this age group; the reasons for this are not known.
  - Children younger than 6 years may have increased glutathione synthesis and turnover.
- Overall, acetaminophen-related fulminant hepatic failure and mortality are rare and tend to be associated with delays in initiating therapy.

CLINICAL PRESENTATION

History

- It is often possible to obtain history of ingestion. As with all potentially toxic exposures, the clinician should inquire specifically about the following:
  - Time of ingestion
  - Liquid, tablet, or sustained-release preparation
  - Exact preparation ingested (so that effects of a coingestant may be anticipated)
  - Quantity ingested
  - Where the ingestant was stored
  - Degree of supervision at the time of ingestion
  - History of prior ingestions
  - Nature of ingestion (intentional versus accidental)
- Risks of unintended, inappropriate dosing include using an adult preparation, using an incorrect measuring device, using a sustained-release preparation, use in combination with cold or pain medications that also contain acetaminophen, administration by another child, or rectal administration.
- Risks that may contribute to toxicity at appropriate doses include genetic polymorphisms involving the cytochrome P450 enzyme system, decreased oral intake, protein-calorie malnutrition, poorly controlled diabetes, chronic liver disease (by prolongation of elimination half-life), and exposure to cytochrome P450-inducing drugs (e.g., carbamazepine, phenobarbital, rifampin, isoniazid [INH]).
- If an acute over-ingestion history cannot be obtained, inquire about recent routine Tylenol dosing, because chronic over-ingestion of acetaminophen can result in clinical toxicity.
- Generally, acute ingestion of more than 120 to 150 mg/kg in pediatric patients or more than 6 g in adult-sized patients is considered potentially toxic. In chronic over-ingestion, 150 to 175 mg/kg, taken over 2 to 4 days, can result in toxicity.
  - Acetaminophen toxicity should be considered in the differential diagnosis when evaluating any patient with anorexia, nausea, and vomiting.
  - Acetaminophen toxicity should be considered with serum transaminase elevation or other liver function abnormalities (as occurs later in the course).
- Many experts advocate routinely obtaining serum acetaminophen levels on all patients presenting with potentially significant ingestion of any kind because acetaminophen is a common coingestant.

Physical Examination

- Initially, patients may be asymptomatic.
- The first symptoms are anorexia, nausea, and vomiting. At 24 to 72 hours, patients may develop right upper quadrant pain.
- Serum transaminase levels often start to increase.
- Prolongation of the prothrombin time (PT) and elevation of the total bilirubin level may be seen.
- Oliguria may develop during this period.
- Further clinical evidence of hepatic dysfunction typically peaks at 72 to 96 hours.
  - Jaundice
  - Excessive bleeding
  - Encephalopathy
- Acute renal failure may also develop during this period.
- After 96 hours, the severely toxic patient may develop irreversible hepatic failure.
  - The ultimate outcome is usually known by 2 weeks after ingestion.
  - Complete recovery of hepatic function is expected in most appropriately treated patients.
- The clinical picture may be dominated early on by the effects of the coingestant (e.g., anticholinergic effects from combination cold preparations, respiratory depression from combination pain medications).

ETIOLOGY

- Hepatotoxic effects result from cytochrome P450 metabolism of acetaminophen to a toxic metabolite, *N*-acetyl-*p*-benzoquinoneimine (NAPQI).
  - It binds irreversibly to liver proteins to cause centrilobular hepatic necrosis unless it is conjugated with endogenous glutathione.
- Other pathways available for APAP metabolism include the following:
  - Sulfation (predominant in neonates)
  - Glucuronidation (a well-developed pathway by 3 years of age)
- Factors important in the development of acetaminophen-related hepatotoxicity include the following:
  - Over-ingestion of acetaminophen
  - Decreased capacity for metabolism by means of glucuronidation or sulfation
  - Increased activity of the cytochrome P450 system
  - Glutathione depletion

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute gastroenteritis
- Viral hepatitis
- Other toxic or chemical hepatitis
- Reye's syndrome
- Inborn error of metabolism
- Wilson disease
- α_1-Antitrypsin deficiency

LABORATORY TESTS

- The serum acetaminophen level should be determined at 4 hours after ingestion.
  - An 8-hour level may also be helpful, especially in cases of exposure to sustained-release acetaminophen preparations.
  - The relationship of initial and subsequent serum levels to time of ingestion should be interpreted according to the Rumack-Matthew nomogram.
  - Four-hour serum levels between 150 and 200 μg/mL are potentially toxic, and 4-hour levels in excess of 200 μg/mL are probably toxic.
- Obtain serum chemistries, including blood glucose, blood urea nitrogen (BUN), the creatinine level, and baseline serum transaminases, ammonia level, PT, and partial thromboplastin time (PTT).
- Consider obtaining serum levels of other common coingestants, such as a salicylate (aspirin).

- Broad-spectrum urine or serum toxicology screens are of uncertain value in acute management.
- Evidence of a significant coingestion is usually clinically apparent.

- In cases of potentially toxic ingestion, hepatic function status should be monitored by obtaining levels of serum transaminases and the PT and PTT (the PT is primarily affected) at 24 hours after ingestion and periodically thereafter if a laboratory abnormality has developed.
  - Special attention should be given to monitoring hepatic function in patients who are at high risk for development of hepatotoxicity.
  - Clinical or laboratory evidence of hepatic dysfunction is usually evident by 48 to 72 hours after ingestion.
- Clinical and laboratory markers of renal function should also be followed because renal failure may develop in the presence or absence of hepatic failure.

TREATMENT

Rx

NONPHARMACOLOGIC THERAPY

Maintain the airway, assist ventilation if necessary, and support intravascular volume.

ACUTE GENERAL Rx

- For initial gastrointestinal decontamination, a single dose (1g/kg body weight) of activated charcoal should be administered within 6 to 8 hours after the ingestion.
  - Activated charcoal adsorbs acetaminophen effectively in the gastrointestinal tract.
  - Many experts believe that it can be given concurrently with the first dose of oral *N*-acetylcysteine (NAC) with no appreciable loss of NAC activity.
- While awaiting the initial serum level, if significant ingestion is suspected or if the 4-hour level is 150 µg/mL or more (or if the initial level relative to time of ingestion falls above the lower line in the Rumack-Matthew nomogram), specific antidotal therapy with 20% oral NAC (Mucomyst) or 20% intravenous acetylcysteine (Acetadote, Cumberland Pharmaceuticals) is indicated.
  - NAC decreases the potential for ongoing hepatotoxicity by acting as a glutathione substitute, by enhancing glutathione stores, and by enhancing metabolism by the alternative sulfation pathway.
  - When given orally, the initial dose is 140 mg/kg, and complete treatment consists of 17 subsequent enteral doses of 70 mg/kg. Doses are given at 4-hour intervals.
- Ondansetron and high-dose metoclopramide have been used with some success to control vomiting.
  - Because of its noxious odor and taste, oral NAC often potentiates ongoing nausea and vomiting.
  - Vomiting caused by the acute ingestion should be controlled as much as possible, because ongoing emesis interferes with administration of appropriate oral treatment.
- In January 2004, the U.S. Food and Drug Administration (FDA) approved an intravenous formulation of NAC (Acetadote, Cumberland Pharmaceuticals) for the treatment of suspected acetaminophen toxicity in adults and children.
  - This preparation is especially useful for patients who cannot tolerate enteral dosing.
  - Patients presenting within 8 to 10 hours of the ingestion should receive a loading dose, followed immediately by a maintenance infusion.
    - Loading dose: 150 mg/kg given intravenously over 15 minutes
    - Maintenance dose: 50 mg/kg given intravenously over 4 hours
    - Continued maintenance dose: 100 mg/kg given intravenously over 16 hours
  - A variable incidence of anaphylactoid reactions has been reported with the use of intravenous NAC.
    - It may be dose related.
    - Most reported cases have been easily managed with symptomatic therapies.
    - Lowering the infusion rate may be considered in these cases.
    - Individuals with a history of bronchospasm may be at increased risk for serious anaphylactic reactions to intravenous NAC.
    - Asthmatics were more likely to develop systemic side effects, but these events were not more severe.
  - Maximal benefit is derived from NAC if it is administered before the toxic metabolite of acetaminophen accumulates or within 8 to 10 hours of acute ingestion.
    - Although it may be of diminishing value in protecting against hepatotoxicity if initiated later, NAC should still be initiated, even if presentation is delayed beyond 24 hours after ingestion.
    - Some experts believe that oral NAC is more effective than intravenous NAC when presentation is longer than 16 hours after ingestion.

CHRONIC Rx

- Hepatic transplantation may be necessary in rare cases.
- Patients who develop severe acidosis, coagulopathy, or encephalopathy may be candidates for transport to a transplant facility.

DISPOSITION

- All patients with intentional ingestions should receive a psychiatric evaluation and treatment after they are medically stable.
- In cases of accidental ingestion, a consultation with a social worker is often helpful to assess the degree of supervision in the home.

REFERRAL

- In general, all patients suspected of having a potentially toxic exposure should be stabilized immediately and then referred to the nearest tertiary care facility with experience in managing critically ill children.
- The nearest regional poison center should be consulted in all cases of intentional or accidental toxic ingestion.

PEARLS & CONSIDERATIONS

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COMMENTS

- Oral NAC may be better tolerated if given by nasogastric tube or if diluted to at least 5% by mixing 1 part of the 20% stock formulation with 3 parts cola or juice. The addition of ice may improve compliance with the regimen.
- Serum levels of acetaminophen may be falsely elevated if the patient also ingested salicylate compounds, cephalosporins, or sulfonamides.

PREVENTION

- The danger of accidental poisoning in the home should be discussed routinely at pediatric health supervision visits, beginning at the 6-month visit.
- Parents should be instructed to childproof the home, including locking all medications and other toxic products out of the reach of children.
- Parents should be provided with the phone number of the regional poison center.
- Parents should be instructed to call the poison center immediately when they suspect that an inappropriate ingestion has occurred.
- Parents should be cautioned that many over-the-counter cold preparations contain acetaminophen and that these should not be given concurrently with acetaminophen.
- Rectal acetaminophen should be avoided because peak drug levels vary and the appropriate dosing interval may be longer than 4 to 6 hours. Parents should also avoid dividing suppositories because the medication is often not evenly distributed within them.

PATIENT/FAMILY EDUCATION

- Parents should be educated about the potential toxicity of acetaminophen (and preparations containing acetaminophen) in the home. These and other medications should be kept in a locked cabinet and out of reach of children, even if they are packaged with childproof caps.

- Families should be provided with the phone number (1-800-222-1222) of the nearest regional poison center.

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BASIC INFORMATION

DEFINITION

Acne vulgaris is a disorder of the hair follicle and sebaceous gland affecting most people during adolescence or young adulthood.

SYNONYM

Comedonal acne

ICD-9-CM CODE
706.1 Acne vulgaris

EPIDEMIOLOGY & DEMOGRAPHICS

- Most common skin disease, affecting nearly 80% of people at some time between the ages of 11 and 30 years
- Most prevalent during adolescence, with greater severity in males

CLINICAL PRESENTATION

- Located in areas of highest sebaceous gland concentration; therefore the face, chest, and back are common sites of involvement.
- Ninety-eight percent of patients with acne have facial involvement; a smaller percentage have involvement on back and chest.
- Classic lesions are open and closed comedones (blackheads and whiteheads), formed by sebum-plugged pilosebaceous follicles.
- Inflammatory papules, pustules, and cysts develop after proliferation of *Propionibacterium acnes* in noninflammatory comedones, with rupture of contents into surrounding dermis.
- Cystic acne manifests by fluctuant and painful nodules and cysts that heal with postinflammatory pigment changes and scar formation.

ETIOLOGY

- There is a multifactorial etiology.
- Androgen production causes increasing sebum levels.
- Obstruction of pilosebaceous follicles is caused by excessive sebum combined with desquamated epithelial cells from follicle.
- *P. acnes* proliferates in an environment of excessive sebum and follicular cells.
- Inflammation is caused by mediators and chemotactic factors produced by bacteria.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Papular scars
- Eosinophilic folliculitis
- Syringomas
- Adenoma sebaceum
- Drug eruption (lithium, corticosteroids)

WORKUP

Diagnosis is usually made on the basis of a characteristic clinical picture.

TREATMENT

NONPHARMACOLOGIC THERAPY

- Wash with mild soap (Dove, Purpose, Neutrogena, Basis) one to two times a day.
- Apply mild moisturizer (Cetaphil, Purpose, Moisturel) as needed.
- Avoid rubbing and scrubbing, which may worsen the condition.

ACUTE GENERAL Rx

All treatments are for several months.

CHRONIC Rx

- No single agent addresses all etiologic factors.
- Combination regimens are the mainstay of treatment.
- Benzoyl peroxide is antibacterial and comedolytic.
  - Available in 1% to 10% gels, creams, pads, and cleansers.
  - Also available in combination with erythromycin (Benzamycin) or clindamycin (BenzaClin, Duac).
  - Use one to two times a day.
  - Side effects include burning, erythema, dryness or peeling, and staining of clothes.
- Topical antibiotics are antibacterial and anti-inflammatory.
  - Erythromycin is available as a solution, gel, ointment, and pad.
  - Clindamycin is available as a solution, gel, lotion, foam, and pad.
  - Use one to two times per day.
  - Side effects include erythema, peeling, and drying.
- Topical retinoids increase cell turnover in the follicle wall and thereby allow expulsion of keratin plugs from microcomedones.
  - Available in many concentrations and forms (cream, gel, microsponge).
  - Begin with lowest concentration and slowly increase if needed.
  - Apply small amount (pea-size for full face) every night.
  - Side effects include transient worsening of acne, irritation, and photosensitivity.
- Systemic antibiotics have an antibacterial and anti-inflammatory mechanism of action.
  - The goal is 2 to 3 months of therapy and then tapering as topical agents are continued.
  - Tetracycline is administered as 500 mg twice a day (take on empty stomach).
  - Erythromycin is administered as 500 mg twice a day (can cause stomach upset).
  - Minocycline is administered as 50 to 100 mg twice a day (can cause hyperpigmentation, autoimmune hepatitis, lupus-like syndrome).
  - Doxycycline is administered as 50 to 100 mg twice a day (can cause sun sensitivity).
- Hormonal therapy (oral contraceptive pills) may be used.
  - A low-dose oral contraceptive containing nonandrogenic progestin, such as norgestimate or desogestrel, may be effective (Ortho-Tri-Cyclen or Yasmin).
  - Treatment for 2 to 4 months is required before any improvement occurs.
- Isotretinoin (systemic retinoids) may be used specifically with consultation of dermatologist.
  - It is indicated for severe nodulocystic acne.
  - It decreases sebum production.
  - It decreases "stickiness" of follicular cells.
  - Side effects include severe teratogen, increased triglycerides, dry skin and mucous membranes, decreased night vision, hyperostosis, and pseudotumor cerebri.
  - Usual course is 20 to 24 weeks.

PEARLS & CONSIDERATIONS

COMMENTS

- The dark color of a blackhead results from oxidized lipids, melanin, and densely packed keratinocytes, not dirt.
- Stress may aggravate acne, but it is not a major primary factor.
- There is no proven link between acne and diet.
- Strains of *P. acnes* that are less sensitive to antibiotics have become more prevalent.

SUGGESTED READINGS

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BASIC INFORMATION

DEFINITION

Adjustment disorder comprises emotional or behavioral symptoms occurring within 3 months of a stressor and lasting no more than 6 months after the stressor or its consequences end. Adjustment disorder involves the inability to adapt to or maladaptive reactions to identifiable stressors, leading to an inability to function normally.

SYNONYMS

Adjustment reaction
Situational reaction

ICD-9-CM CODES
309.00 With depressed mood
309.3 With disturbance of conduct
309.9 Adjustment disorder (unspecified)
309.24 With anxiety
309.28 With mixed anxiety and depression

EPIDEMIOLOGY & DEMOGRAPHICS

- Adjustment disorders are common.
- Prevalence has been estimated at 2% to 8% in children and adolescents.
- There is no gender difference in the incidence of adjustment disorders.
- Adjustment disorders are more common in disadvantaged circumstances.

CLINICAL PRESENTATION

- Inciting stressor should be evident.
- Depressed mood is common.
- Anxiety is common.
- Sleep abnormalities may exist.
- The patient should have been asymptomatic before the inciting stressor occurred.
- Physical examination results do not contribute to the diagnosis.
- Distress exceeds that expected by the nature of the stressor, or distress results in significant social, academic, or occupational impairment.
- The disorder is not caused by bereavement (which should be diagnosed if appropriate).

ETIOLOGY

- Similar stressors may vary across cultures in their impacts and consequences.
- Responses may be familial (genetic and learned) and situational.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Many psychiatric conditions are triggered by stressors.
- Diagnose adjustment disorder only when the following are not predominant:
  - Mood disorder
  - Anxiety disorders
  - Bereavement
  - Posttraumatic stress disorder (PTSD)
- If personality disorders acquire new symptoms in response to a stressor, an additional diagnosis of adjustment disorder may be appropriate.

WORKUP

A thorough history is needed to exclude alternative diagnoses.

TREATMENT

NONPHARMACOLOGIC THERAPY

- Attempts to change the environment and to remove the stressor are more likely to succeed than therapy alone.
- Vigorous emotional support is desirable; insight may or may not be helpful.

ACUTE GENERAL Rx

Brief use of benzodiazepines or antihistamines may help, but prolonged use should be avoided.

CHRONIC Rx

Repeated episodes imply a different diagnosis (e.g., anxiety disorder, mood disorder) and suggest family therapy and environmental change as alternatives to repeated crisis services.

DISPOSITION

Environmental or situational changes may alleviate symptoms adequately.

REFERRAL

Referral is usually not required in true adjustment disorder because, by definition, it is an acute situational response.

PEARLS & CONSIDERATIONS

COMMENTS

- This diagnosis is often chosen in the misguided hope that a condition is transient. Choosing the diagnosis is frequently a measure of the clinician's wish to dismiss troublesome situations in crisis-oriented, unmotivated families.
- The diagnosis is misused when symptoms have existed for many months or even years.

PREVENTION

- There is little practical advice about prevention of this condition.
- Altering ongoing predisposing factors may prevent recurrent episodes.

PATIENT/FAMILY EDUCATION

Individual and family therapy may help avoid subsequent episodes.

SUGGESTED READINGS

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BASIC INFORMATION

DEFINITION

Adrenal insufficiency is the impaired secretion of adrenocorticoid steroid hormones as a result of adrenal dysfunction or lack of adrenocorticotropic hormone (ACTH) from the pituitary. *Addison's disease* is the term used to refer to acquired adrenal insufficiency caused by adrenal gland destruction.

SYNONYMS

Addison disease
Adrenocorticoid insufficiency
Hypercortisolism

ICD-9-CM CODE
255.4 Addison's disease, adrenal insufficiency

EPIDEMIOLOGY & DEMOGRAPHICS

- The disorder is not well defined in children, and adults are most often affected.
- The prevalence is 1 case per 100,000 people.
- The incidence of X-linked adrenoleukodystrophy is 1 case per 20,000 people.

CLINICAL PRESENTATION

History

- The presentation may be acute or chronic.
- Symptoms may include any of the following:
  - Weakness
  - Fatigue
  - Fever
  - Abdominal pain
  - Anorexia
  - Nausea
  - Vomiting
  - Easy tanning or frank hyperpigmentation
  - Symptoms of hypoglycemia
- Salt craving may occur if the patient is mineralocorticoid deficient.

Physical Examination

- General: thin, fatigued appearing
- Vital signs
  - Orthostatic hypotension
  - Hypotension or shock
  - Tachycardia
- Signs of dehydration
  - Dry mucous membranes
  - Sunken eyes, fontanelle
  - Lethargy, skin tenting
  - Tachycardia
- Skin: hyperpigmentation in primary adrenal failure with high ACTH levels
  - Most obvious around skin creases, nipples, lip borders, buccal mucosa, nailbeds, and areas not exposed to light

ETIOLOGY

- Primary (adrenal pathology)
  - Congenital adrenal hypoplasia
    - *NR0B1* (formerly designated *DAX1*) gene deletion or mutation
    - An X-linked form associated with hypogonadotropic hypogonadism
    - Sometimes part of contiguous gene deletion syndrome with Duchenne's muscular dystrophy or glycerol kinase deficiency
  - Congenital adrenal hyperplasia
    - Usually caused by an autosomal recessive 21-hydroxylase deficiency
  - ACTH unresponsiveness
    - Occasionally associated with achalasia and alacrima
  - Autoimmunity
    - Most common cause in adults
    - May be isolated but is often associated with one of the following syndromes: autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED) or polyglandular autoimmune syndrome (PGA) type I, which is associated with mucocutaneous candidiasis, hypoparathyroidism, and occasionally with type 1 diabetes or hypothyroidism
  - Adrenoleukodystrophy (ALD)
    - X-linked disorder in which progressive central demyelination causes neurologic manifestations starting in the late first decade of life
  - Associated infections
    - Tuberculosis
    - Histoplasmosis
    - Sarcoidosis
    - Acute adrenal hemorrhage in meningococcemia or other bacterial infection (i.e., Waterhouse-Friderichsen syndrome)
- Secondary and tertiary (pituitary or hypothalamic) adrenal insufficiencies caused by ACTH deficiency
  - Pituitary or hypothalamic tumor
  - Congenital hypopituitarism or isolated ACTH deficiency
  - Postoperative or postradiation therapy
  - Suppression after long-term glucocorticoid use (usually not a problem if glucocorticoid therapy is administered for less than 2 consecutive weeks)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nonspecific and vague nature makes the differential diagnosis large and variable, depending on the presentation.
- Gastrointestinal complaints may mimic inflammatory bowel disease, celiac disease, malignancy, or anorexia nervosa.
- Fatigue, depression, and behavioral changes may mimic depression and other psychological conditions.

LABORATORY TESTS

- Serum levels of electrolytes and glucose
  - Low sodium and high serum potassium levels are common if aldosterone deficiency is present.
  - Acidosis may be seen.
  - Hypoglycemia is common.
- Cortisol level (morning sample): low serum cortisol (less than 10 μg/dL) on morning sample
- ACTH level: high ACTH level in primary adrenal failure, inappropriately low for cortisol level in secondary (pituitary) hypoadrenalism
- Renin level: high renin level if aldosterone deficiency is present
- ACTH stimulation test: Administer 0.25 μg of ACTH 1-24 (Cortrosyn) intravenously with cortisol levels at 0 and 60 minutes (not necessary if morning cortisol low with high ACTH level). Level should rise to above 15 to 20 μg/dL after ACTH stimulation.
- Adrenal antibodies or 21-hydroxylase antibodies in autoimmune adrenalitis

IMAGING STUDIES

- Radiographic studies
- Possible adrenal imaging by computed tomography or magnetic resonance to assess size, consistency, and presence of mass

TREATMENT

ACUTE GENERAL Rx

- Acute (adrenal crisis)
  - Intravenous fluids: bolus of normal saline if the patient is hemodynamically unstable; then rehydration rate of normal saline with 5% dextrose
  - Intravenous glucocorticoids: bolus of 100 mg of injectable hydrocortisone (e.g., Hydrocortone Phosphate) and then infusion at 100 mg/m^2/day
  - Mineralocorticoids
    - Not needed initially because high-dose hydrocortisone effectively replaces mineralocorticoid
    - Not generally needed in secondary adrenal insufficiency (i.e., ACTH deficiency)
- Stress dosing
  - Illnesses without vomiting: Three to five times the usual oral dose is needed for the duration of illness (hydrocortisone, approximately 50 mg/m^2/day).
  - Illness with vomiting: parenteral administration of stress-dose glucocorticoids

CHRONIC Rx

- Long-term therapy
  - Glucocorticoid: hydrocortisone taken orally at 15 to 20 mg/m^2/day (optimal may be less)
  - Mineralocorticoid: Florinef (9α-fluorocortisol) at 0.05 to 0.20 mg/day
- Stress dosing
  - Illnesses without vomiting: Three to five times the usual oral dose is needed for