

Practical Psychiatry in Medicine

Part 15. Schizophrenic Disorders

Schizophrenia refers to a group of conditions characterized by disturbances of thought, affect, and behavior that lead eventually to a wide variety of signs and symptoms, such as social and emotional withdrawal, mood disturbances, periods of excitement and immobility, misinterpretations of reality, delusions, and hallucinations. Although the constellation of signs and symptoms comprising a schizophrenic syndrome is often unmistakable, there is no single sign or symptom that is pathognomonic of schizophrenic illness.

Schizophrenic illness usually begins during adolescence or young adulthood. The incidence of new cases in the United States among people age 15 and above is estimated at between 0.3 and 1.2 per 1000 per year.³ Because of the early age at onset, the seriousness of the disorder, and its tendency to be chronic or recurrent, schizophrenic illness accounts for one-third to one-half of the beds occupied in psychiatric hospitals. All races and socioeconomic groups are affected, but the prevalence is higher among the poor.

In recent years it has become increasingly important for the primary physician to be familiar with these disorders. This is true for several reasons. Since the advent of effective chemotherapy, more schizophrenic patients are able to live outside the hospital. As a result

the physician is now much more apt to be consulted in the clinic or in his office by the schizophrenic patient who happens to have an incidental medical problem or whose emotional disturbance manifests itself in somatic symptoms or concerns. Further, potent chemotherapeutic agents, sometimes in very high dose, are commonly used in the management of schizophrenic illness. The physician may be involved in the management of patients who exhibit side effects or toxic reactions to these drugs. He must be knowledgeable of the condition for which these agents are used so that he may have some idea of what to look for if chemotherapy must be discontinued. Finally, and most importantly, it is usually the family physician to whom the patient and/or his family first turn for help in the early stages of the illness, and whose advice and counsel will continue to be sought during the often prolonged course of psychiatric treatment.

Etiology

There is no single cause of schizophrenia. In the past, various theories of etiology have competed, but now, as with many other diseases, schizophrenia is considered to be the result of several interacting factors.

Genetic Factors

Genetic studies have repeatedly indicated that the concordance for schizophrenia is significantly higher among pairs of monozygotic twins

than among pairs of dizygotic (fraternal) twins. In addition, recent studies of schizophrenics who were adopted at birth into nonschizophrenic families have found higher incidence of schizophrenia among the biologic relatives (parents, siblings, or half-siblings) than among the general population.⁷

Biochemical Factors

The genetic factor is probably mediated by a biochemical change or set of changes. Here, only hypotheses have so far been offered, with no clear proofs. For example, dopamine has been implicated in Snyder's hypothesis,¹¹ since phenothiazines and other antipsychotic medications block dopamine receptors (this probably accounts for the production of parkinsonism as a side effect). In addition, dextroamphetamine, which can exacerbate schizophrenic psychoses or induce a schizophrenia-like illness when given in large doses, increases the activity of neurotransmitters at dopaminergic as well as noradrenergic synapses in the central nervous system.

Early Environmental Influences

Family experiences during childhood no doubt sometimes play a part in the development of schizophrenia, but the clearcut descriptions of a decade ago of the schizophrenogenic mother or of specific pathologies in the families of schizophrenic patients have not

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The following chapter has been selected by the Publisher from its book, *Practical Psychiatry in Medicine*, by John B. Imboden, MD, and John Chapman Urbaitis, MD, in the hope that it will have immediate usefulness to our readers.

Continued from preceding page

held up. On the other hand, it does seem clear that such factors as marked parental inconsistency, ambiguity of communications with the child, and failure to provide adequate role models or an atmosphere of love acceptance are all likely to impair personality development and thus intensify the stressfulness of life. This may be of great importance in the individual genetically predisposed to schizophrenic illness.

Current Stress

Stress resulting from current psychologic and social pressures frequently appears to play a role in schizophrenic decompensation. It has long been noted, for example, that the illness often makes its appearance at the transitional junctures of adolescence or young adulthood.

In sum, then, while etiology is far from fully understood, it does appear that the several factors of genetic predisposition, biochemical malfunctions, early environmental influences, and current stress all contribute to the development of schizophrenic illness.

Clinical Characteristics

Mode of Onset

In some patients there is a preillness history of shyness, oversensitivity, emotional inhibition, and a tendency to daydream and to be a loner. Many patients, however, do not have such a history and many persons who do have such a history

never become afflicted with a schizophrenic illness.⁹

The onset may be insidious, sometimes consisting initially in progressive withdrawal from friends and family, decline in academic interest and achievement, hypochondriacal preoccupations, multiple somatic complaints, and neurotic symptoms such as obsessions and compulsions. In this insidious mode of onset months may go by before the family realizes that something serious is going on, and this realization may not occur until some bizarre, disturbing behavior develops.

In other patients, the illness develops more rapidly and dramatically, the patient exhibiting such unmistakable evidences of profound disturbance as psychomotor excitement, panic, marked alteration of mood, delusions, and hallucinations. The initial development and subsequent exacerbations of schizophrenic illness may or may not be associated with stressful events or situations. As already noted, often the illness tends to develop or worsen around transitional periods of youth: puberty, adolescence, graduation from high school or college, leaving home or school and facing the prospects of going out into the world.

Disturbance of Affect

The affective manifestations of schizophrenic illness are manifold and vary greatly from one patient to the next and in the same patient over a period of time. Not infrequently the patient exhibits a reduction or "flattening" of affect: this feature may be associated with a progressive diminution or narrowing of interests and loss of ability to experience pleasure or deep

satisfaction in any activity or interpersonal relationship. This anhedonic state often leads the patient to feel empty, isolated, and lost; he may despair of ever being better and may contemplate suicide. Affective flatness and withdrawal may make the patient seem exasperatingly indifferent to everything and everybody.

The patient may also display affect that seems silly or inappropriate to what he is talking about or to his situation. He may, especially early in the illness, have a burst of emotion accompanied by sudden conviction that "everything is clear" about previously mysterious events.¹ The patient may have periods of melancholy, elation, irritability, anger, and fearfulness.

Disturbance of Cognitive Functions

Evidence of cognitive disorder may be revealed in difficulties in communication, and in the development of delusions and hallucinations.

Communication

In normal communication, one attempts to convey a concept to the listener. In doing this, one must often relate background material or subordinate concepts in order to get the main idea across. Thus, normal communication requires the speaker, on the one hand, to be in touch with associations relevant to the idea he is communicating and, on the other hand, to screen out those which are irrelevant. In schizophrenic thought disorder there may be difficulty with either

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or both of these processes, ie, severe inhibition of associations or failure in screening out tangential and irrelevant associations. Both of these difficulties may result in speech that is poorly connected or fragmented, ie, in what is often referred to as "loosening" of associations.

When the associative processes are severely constricted the patient may find that his thoughts are frequently "blocked" so that he loses his train of thought. Constriction of associations may be revealed in a tendency to concrete thinking as manifested by very narrow, literal interpretations of simple proverbs. The patient may indicate that he feels he has no thoughts and may indicate that his thoughts have been taken from him by an outside agency.

On the other hand, failure to screen out irrelevant or tangential associations often occurs and may result in excessively circumstantial speech; in extreme cases, the patient never seems to get to the point—his speech is rambling, vague, and difficult or impossible to follow. He may be strikingly overinclusive when asked a straightforward question or when confronted with a simple task or problem.

Other disturbances of communication include the idiosyncratic use of words, creating new words (neologisms), repeating words or phrases in a stereotyped fashion, and negativism.¹⁰

Delusions

Everyone's judgment, beliefs, reasoning, and even perceptions are influenced to a degree by cur-

rently prevailing emotions, especially wishes and fears. In a state of intense fear, for example, one may interpret innocuous shadows and sounds as having some ominous significance. In patients with schizophrenic illness, cognitive functions may be abnormally vulnerable to such influences as wishes and fears.

Many schizophrenic patients tend to be preoccupied with the fear of being controlled or influenced by other persons or "outside forces." It is possible that in some cases this apparent fear represents an underlying wish. In any event it is not uncommon for the patient to express the notion that he is being kept under surveillance, is followed when he walks down the street, that thoughts are being inserted into or withdrawn from his mind, that his behavior is being directed by someone, that bodily sensations are being imposed upon him. He may have the delusion that he is being persecuted. The patient's delusions may be elaborate and well systematized (internally consistent) or they may be unelaborated or fragmented.

Preoccupation with the self, and absorption in his own fantasies and bodily processes are characteristically present. This narcissistic orientation in conjunction with defensiveness concerning feelings of loneliness, inadequacy, and guilt may lead to a variety of delusions. Notions of grandiosity are often seen, particularly in patients who feel they are the target of a conspiratorial plot. Ideas of reference occur in which the patient believes that he is the subject of news articles, television programs, and so forth. Somatic delusions, sometimes buried in what superficially looks like a hypochondriacal neurosis, are not rare.

Sometimes, the outer world seems distant, strange, and unreal (derealization) and sometimes he himself feels unreal (depersonalization). The patient may identify the cosmos with himself and, fearing the dissolution of his own mind, have the conviction that the end of the world is nigh.

Hallucinations

In schizophrenic illness, hallucinations involving any sensory modality may occur, but usually they are predominantly auditory. Auditory experiences of several types are found. Voices may be heard which are discussing the patient and which refer to him in the third person, or which describe or comment on the patient's activities as they take place. The patient may have the experience of hearing his own thoughts, as though aloud but within his head ("gedankenlautwerden").¹⁰

Behavior

As one may infer from the above description of the profound disturbances in affect and cognition, schizophrenic patients may show a wide variety of behaviors which range from the mildly eccentric to the bizarre. Many schizophrenic patients are obviously ill at ease with other people and may seem awkward or gauche in social situations. An air of guardedness or suspiciousness is common in patients with paranoid tendencies. On the other hand, some schizophrenic patients may not reveal any particular behavioral clues of their

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illness in casual social situations, while nonetheless revealing unmistakable pathology when carefully interviewed or when observed over a period of time.

Particularly striking alterations of psychomotor behavior are catatonic stupor and catatonic excitement. In the former state the patient is immobile, sitting or standing in same position for hours, not speaking or eating; in catatonic stupor, the patient's hand or arm remains in the position in which it is passively placed (waxy flexibility). In catatonic excitement, the patient may lose control of aggressive impulses and may strike out suddenly at people and things in his immediate environment; the patient may be generally overactive, running around wildly and talking incoherently.

Classification

There are several ways of classifying the various subtypes of schizophrenia. We will consider only three.

The Classic Syndromes of Kraepelin and Bleuler

The syndromes of Kraepelin and Bleuler do not occur in as pure and stable a form as one would infer from the early descriptions of schizophrenia.^{9,10} The comparative rarity of these syndromes "in pure form" is in part due to the influence of modern chemotherapy. The classic syndromes referred to are as follows.

Paranoid Schizophrenia

In paranoid schizophrenia, ideas of reference, delusions of being watched, followed, or persecuted, and delusions of grandiosity dominate the clinical picture. Onset of the illness tends to be somewhat later than in other forms of schizophrenia, often first becoming manifest in the 30s age group. These patients are often tense, guarded, and suspicious. Typically there is rather good preservation of intellectual function (outside of the delusions) and the patient may be able to function well in many areas of life.

Catatonic Schizophrenia

Catatonic schizophrenia applies to patients whose illness is primarily manifested by the disturbances in psychomotor behavior described above: catatonic stupor and/or excitement. In addition, catatonic patients typically have hallucinatory experiences and delusions as well as psychomotor symptoms.

Hebephrenic Schizophrenia

Hebephrenic schizophrenia typically begins in the teens (Hebe, the Greek goddess of youth). It is a severe disorder characterized by silly, inappropriate affect, hallucinations, poorly organized delusions, and severely regressive behavior.

Simple Schizophrenia

Simple schizophrenia is characterized primarily by *progressive* shallowness of emotion, and reduction in interests and in attachments to things, situations, and people. Patients with this condition show little interest in holding a job or pursuing goals. They may show

little evidence of delusions and hallucinations.

Process-Nonprocess Schizophrenia

It has been found useful to classify schizophrenic illness into two types: one characterized by features associated with a relatively good prognosis (nonprocess type), and the other by features associated with a relatively poor prognosis (process type).¹²

The relatively good prognosis type is characterized by the following: good preillness level of adjustment, presence of stress at time of onset, acute onset, presence of excitement, tension, anxiety, and affective symptoms. Illnesses falling into the good prognosis group may be referred to as nonprocess schizophrenia, reactive schizophrenia, schizoaffective disorder, remitting schizophrenia, and schizophreniform illness.

The group with relatively poor prognosis is sometimes referred to as process schizophrenia or "true" schizophrenia and its characteristics are poor preillness adjustment; slow and insidious onset; absence of precipitating stress; relative lack of tension, anxiety, or affective symptoms; emotional blunting or flatness; and relatively high incidence of schizophrenic illness in the family.

It is important to note that when dealing with individual patients, the prognostic indicators noted above do not always prove to be accurate.⁴ That is, it is imperative to proceed with active treatment and with a hopeful attitude regardless of which group the patient appears to belong to.

Continued on page 944

Continued from page 942

The Classification of Klein and Davis

These investigators have offered a classification of schizophrenia based on presenting symptoms, childhood adjustment, and likely response to medications.⁸ It has the virtues of simplicity and a close connection to the patients as we may encounter them in clinical practice. Klein and Davis have classified schizophrenic disorders into three groups as described below.

1. "Schizophrenia—childhood asociality" is a condition with marked thought disorder, much disorganized thinking (even delusions are vague), and fragmented verbal productions. In affect, these patients are frightened rather than angry or depressed. History of their childhood shows aloof, cold, asocial behavior, with no real friendships. This group of patients is the least likely to respond to treatment, and long-term prognosis is poor.

2. "Schizophrenia—fearful paranoid" presents with a suspicious and defensive patient, who has clear-cut delusions, ideas of reference, and paranoid ideas about other people. Delusions may include beliefs in changes in shape, size, or function of bodily parts. The patient may be depressed or suicidal, especially early in the course of illness. Angry outbursts may occur when the paranoid patient believes himself to be trapped. Childhood is typically not so disturbed, though there may be some pattern of being a loner. These patients are likely to respond to treatment, and the prognosis is fair to good.

3. "Schizophrenia—schizoaffec-

tive" refers to an illness with definite affective psychotic manifestations, resembling either mania or psychotic depression; in addition, the patient must show clear-cut schizophrenic thought disorder with bizarre and/or persecutory delusions. The illness is often of acute onset, and response to treatment is generally good with a favorable prognosis in the long run.

Diagnosis

In its florid form, the diagnosis of schizophrenia usually presents no difficulty. In early stages of the illness, however, especially when the onset is slow and insidious, it may be extremely difficult to make a definite diagnosis until the patient has been observed over a period of time. In such instances, the initial manifestations may consist predominantly of neurosislike symptoms such as hypochondriacal preoccupations, obsessions, and compulsions, or a sort of social maladjustment with such features as decline in school performance, and a progressive tendency to withdraw from interpersonal contacts and to prefer solitary pursuits. Such symptoms occurring in an adolescent or young adult may arouse the suspicion of schizophrenic illness and lead the physician to be alert to the presence of the characteristic disturbances in cognition and affect, perhaps present in relatively subtle or mild form.

With regard to more fully developed schizophrenic disorder, it should be kept in mind that a variety of conditions can be associated

Continued on page 947

Brief Summary of Prescribing Information

Benylin® Cough Syrup

Each 5 ml contains:

Benadryl® (diphenhydramine hydrochloride) 12.5mg
 Alcohol 5%
 Also contains, as inactive ingredients, sugar, water, glucose liquid, glycerin, ammonium chloride, sodium citrate, raspberry imitation flavor, sodium saccharin, citric acid, caramel, menthol; FD&C Red 40, and D&C Red 33.

INDICATIONS. Benylin Cough Syrup is indicated as an antitussive for the control of cough due to colds or allergy.

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified this indication as follows:

There is a lack of substantial evidence that this fixed combination drug has the effect purported. Final classification of the less-than-effective indication requires further investigation.

CONTRAINDICATIONS. Use in Newborn or Premature Infants: This drug should *not* be used in newborn or premature infants.

Use in Nursing Mothers: Because of the higher risk of antihistamines for infants generally, and for newborns and premature infants in particular, antihistamine therapy is contraindicated in nursing mothers.

Use in Lower Respiratory Disease: Antihistamines should *NOT* be used to treat lower respiratory-tract symptoms including asthma.

Antihistamines are also contraindicated in the following conditions:

Hypersensitivity to diphenhydramine hydrochloride and other antihistamines of similar chemical structure.

Monoamine oxidase inhibitor therapy (See Drug Interaction section).

WARNINGS. Antihistamines should be used with considerable caution in patients with narrow-angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder-neck obstruction, or pyloroduodenal obstruction.

Use in Children: In infants and children, especially, antihistamines in *overdosage* may cause hallucinations, convulsions, or death.

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, antihistamines may produce excitation.

Use in Pregnancy: Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus.

Use with CNS Depressants: Diphenhydramine hydrochloride has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).

Use in Activities Requiring Mental Alertness: Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating appliances, machinery, etc.

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

PRECAUTIONS. Diphenhydramine hydrochloride has an atropine-like action and, therefore, should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension.

DRUG INTERACTIONS. MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

ADVERSE REACTIONS. The most frequent adverse reactions are underscored:

1. *General:* Urticaria; drug rash; anaphylactic shock; photosensitivity; excessive perspiration; chills; dryness of mouth, nose, and throat

2. *Cardiovascular System:* Hypotension, headache, palpitations, tachycardia, extrasystoles

3. *Hematologic System:* Hemolytic anemia, thrombocytopenia, agranulocytosis

4. *Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions

5. *GI System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation

6. *GU System:* Urinary frequency, difficult urination, urinary retention, early menses

7. *Respiratory System:* Thickening of bronchial secretions; tightness of chest and wheezing, nasal stuffiness

OVERDOSAGE. Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms—dry mouth; fixed, dilated pupils; flushing; and gastrointestinal symptoms may also occur.

If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

If vomiting is unsuccessful, gastric lavage is indicated within three hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or one-half isotonic saline is the lavage solution of choice. Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and, therefore, are valuable for their action in rapid dilution of bowel content

Stimulants should *not* be used.

Vasopressors may be used to treat hypotension.

HOW SUPPLIED. Benylin Cough Syrup is supplied in 4-oz, 1-pt, and 1-gal bottles, and unit-dose bottles of 5 ml and 10 ml.

May 1978

PARKE-DAVIS

Div of Warner-Lambert Co
 Morris Plains, NJ 07950 USA

PD-JA-2628-2-P(10-79)

PEDIAMYCIN® 400

ERYTHROMYCIN ETHYLSUCCINATE ORAL SUSPENSION

Indications
The mode of action of erythromycin is by inhibition of protein synthesis without affecting nucleic acid synthesis. Resistance to erythromycin of some strains of *Haemophilus influenzae* and staphylococci has been demonstrated. Culture and susceptibility testing should be done. If the Kirby-Bauer method of disc susceptibility is used, a 15 mcg erythromycin disc should give a zone diameter of at least 18 mm when tested against an erythromycin-susceptible organism.

Orally administered erythromycin ethylsuccinate suspensions are readily and reliably absorbed. Pediamycin Chewable is readily and reliably absorbed when chewed. Comparable serum levels of erythromycin are achieved in the fasting and the nonfasting states.

After absorption, erythromycin diffuses readily into most body fluids. In the absence of meningeal inflammation, low concentrations are normally achieved in the spinal fluid, but passage of the drug across the blood-brain barrier increases in meningitis. In the presence of normal hepatic function, erythromycin is concentrated in the liver and excreted in the bile; the effect of hepatic dysfunction on excretion of erythromycin by the liver into the bile is not known. After oral administration, less than 5 percent of the activity of the administered dose can be recovered in the urine.

Erythromycin crosses the placental barrier but fetal plasma levels are generally low.

Contraindications
Streptococcus pyogenes (Group A beta-hemolytic streptococcus): Upper and lower respiratory tract, skin and soft tissue infections of mild to moderate severity.

Infectable benzathine penicillin G is considered by the American Heart Association to be the drug of choice in the treatment and prevention of streptococcal pharyngitis and long-term prophylaxis of rheumatic fever. In treatment of the above conditions, penicillin G (V) or erythromycin is the alternate drug of choice.

When oral medication is given, the importance of strict adherence by the patient to the prescribed dosage regimen must be stressed. A therapeutic dose should be administered for at least 10 days.

Alpha-hemolytic streptococci (viridans group): Short-term prophylaxis of bacterial endocarditis prior to dental or other operative procedures in patients with a history of rheumatic fever or congenital heart disease who are hypersensitive to penicillin. Erythromycin is not suitable prior to genitourinary surgery where the organisms likely to lead to bacteremia are gram-negative bacilli or the enterococcus group of streptococci.

Staphylococcus aureus: Acute infections of skin and soft tissue of mild to moderate severity. Resistant organisms may emerge during treatment.

Streptococcus (Diplococcus) pneumoniae: Upper respiratory tract infections (e.g., sinusitis, otitis media, pharyngitis) and lower respiratory tract infections (e.g., pneumonia) of mild to moderate degree.

Mycoplasma pneumoniae (Eaton agent, P.PLO): For respiratory infections due to this organism.

Haemophilus influenzae: For upper respiratory tract infections of mild to moderate severity when used concomitantly with adequate doses of sulfonamides. Not all strains of this organism are susceptible at the erythromycin concentrations ordinarily achieved (see appropriate sulfonamide labeling for prescribing information).

Regina pallidum: Erythromycin is an alternate choice of treatment for primary syphilis in patients allergic to the penicillins. In treatment of primary syphilis, spinal fluid examinations should be done before treatment and as part of follow-up after therapy.

Corynebacterium diphtheriae and *C. miltitissimum*: As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

In the treatment of erythrasma.

Clostridia histolytica: In the treatment of intestinal amebiasis only. Extra-enteric amebiasis requires treatment with other agents.

Legionnaires' Disease: Although no controlled clinical efficacy studies have been conducted, *in vitro* and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' Disease.

Contraindications
Erythromycin is contraindicated in patients with known hypersensitivity to this antibiotic.

Warnings
Usage during pregnancy and lactation: The safety of erythromycin for use during pregnancy has not been established.

Erythromycin crosses the placental barrier. Erythromycin also appears in breast milk.

Precautions
Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. There have been reports of hepatic dysfunction, with or without jaundice occurring in patients receiving erythromycin products.

Recent data from studies of erythromycin reveal that its use in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity. In case of theophylline toxicity or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving concomitant erythromycin therapy.

Surgical procedures should be performed when indicated.

Adverse Reactions
The most frequent side effects of oral erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose related. Nausea, vomiting and diarrhea occur infrequently with usual oral doses.

During prolonged or repeated therapy, there is a possibility of overgrowth of non-susceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted.

Mild allergic reactions such as urticaria and other skin rashes have occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Dosage and Administration

Erythromycin ethylsuccinate suspensions and chewable tablets may be administered without regard to meals.

For full therapeutic effect, Pediamycin Chewable tablets must be chewed. They should not be swallowed whole.

Children: Age, weight and severity of the infection are important factors in determining the proper dosage. In mild to moderate infections the usual dosage of erythromycin ethylsuccinate for children is 30 to 50 mg/kg/day in equally divided doses. For more serious infections this dosage may be doubled.

Adults: 400 mg erythromycin ethylsuccinate every 6 hours is the usual dose. Dosage may be increased up to 1 g per day according to the severity of the infections.

If twice-a-day dosage is desired in either adults or children, one-half of the total daily dose may be given every 12 hours. Doses may also be given three times daily if desired administering one-third of the total daily dose every 8 hours.

How Supplied
Pediamycin 400 (erythromycin ethylsuccinate oral suspension) is supplied in 1-pint bottles (NDC 4-0211-16) and 100-ml bottles (NDC 0074-0211-13). It provides erythromycin ethylsuccinate equivalent to 400 mg erythromycin per teaspoonful (5 ml).

Continued from page 944

with delusions, hallucinations, and other symptoms common in schizophrenia; among these are the organic brain syndromes and affective disorders.

Typically, in schizophrenic illness the sensorium is clear and if hallucinations are present it is common for the auditory type to be predominant. In delirium, in addition to clouded sensorium, visual hallucinations often predominate.

Hallucinations and delusions can occur in severe depressive and manic states; in that event their content usually reflects a depressive or expansive attitude toward the self and the future. Other manifestations of affective illness should be sought including a family history of affective illness.

Amphetamine intoxication can closely simulate schizophrenic illness; the diagnosis is made by a history of amphetamine ingestion and by relatively rapid (one to two weeks) symptomatic remission following separation from the drug, which is sustained for as long as the patient abstains from further amphetamine ingestion.

In the diagnostic evaluation of patients with schizophrenic illness, no matter how obvious the diagnosis appears, the physician conducts a careful neurologic and general medical examination just as he does in evaluating patients with other types of illness.

Management

The patient with schizophrenic illness should be referred to the

psychiatrist for continued evaluation and treatment. This does not mean, however, that the primary physician will have no further role in the management of the patient. More often than not, worried parents will consult the primary physician from time to time, even after the psychiatric referral is made, in order to have his opinion about various aspects of the treatment and course of the patient's illness. The parents may feel guilty, as if they are to blame for their son's or daughter's illness, and seek the physician's counsel about their feelings. The parents and the patient may rely on the advice of the primary physician as to whether to accept some specific recommendation, such as hospitalization, that the psychiatrist may have made. For these and other reasons, it is appropriate for the physician to have some general understanding of the psychiatric management of schizophrenic illness, and for the primary physician and the psychiatrist to communicate with each other from time to time about the patient's treatment and progress.

Treatment for schizophrenic patients includes several modalities.⁵ We have previously described patterns of symptoms and the most expected prognosis based on stereotyped descriptions. Now as we consider treatment of the individual patient, however, we are reminded that population statistics do not provide a valid ironclad predictor for outcome in any individual patient. Therefore, each schizophrenic patient should have a vigorous and thorough program of treatment, regardless of the characteristics of his particular illness.

Continued on page 950

ROSS LABORATORIES
COLUMBUS, OHIO 43216
Division of Abbott Laboratories, USA

Fastin® 30 mg. (V) (phentermine HCl)

Before prescribing FASTIN® (phentermine HCl), please consult Complete Product Information, a summary of which follows:

INDICATION: FASTIN is indicated in the management of exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate-to-severe hypertension, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma, agitated states.

Patients with a history of drug abuse.
During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

FASTIN may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: FASTIN is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of FASTIN should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Use of FASTIN by women who are or who may become pregnant, and those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: FASTIN is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing FASTIN for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of FASTIN and the concomitant dietary regimen.

FASTIN may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure. *Central Nervous System:* Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria. *Endocrine:* Impotence, changes in libido.

DOSAGE AND ADMINISTRATION: *Exogenous Obesity:* One capsule at approximately 2 hours after breakfast for appetite control. Late evening medication should be avoided because of the possibility of resulting insomnia.

Administration of one capsule (30 mg.) daily has been found to be adequate in depression of the appetite for twelve to fourteen hours. FASTIN is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage with phentermine include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute phentermine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard. Acidification of the urine increases phentermine excretion. Intravenous phentolamine (REGITINE) has been suggested for possible acute, severe hypertension, if this complicates phentermine overdosage.

CAUTION: Federal law prohibits dispensing without prescription.

SCHIZOPHRENIC DISORDERS

Continued from page 947

The overall goals of treatment are reduction of the duration and degree of disability for each patient in each episode of illness, and limitation of the impact of the patient's illness on family and community. Subsidiary objectives in planning for these goals include reduction of psychotic symptoms, decreasing the disruption of personal life, and finding ways to prevent future relapses.

The means of treatment are a network or system of services. Just as the illness has developed within the context of a person's life, so treatment must be planned to fit into that context or skillfully to alter the context of the patient's life. Psychiatrists, psychiatric outpatient clinics, psychiatric hospital services, and social work and rehabilitation programs all collaborate in providing continuity of clinical services. A single person must coordinate these joint efforts; sometimes this person is the psychiatrist, sometimes the family physician.

Techniques of treatment can be divided into three categories: chemotherapy, psychotherapy, and social therapy.

Chemotherapy

Chemotherapy has become the mainstay of therapy for schizophrenia.^{2,8} Antipsychotic drugs have been demonstrated as markedly more effective than placebos in promoting recovery from acute episodes of schizophrenic psychosis. Psychotic symptoms are disruptive to the patient and to those around him, and the judicious use of adequate doses of antipsychotic

medications can do much to relieve the suffering.

A number of antipsychotic drugs are available, and their major actions are similar. Choice of a particular one depends on the secondary effects or side effects, and on the patient's responses. The less potent phenothiazines (Thorazine, Mellaril) are more sedating, and tend to have lower incidence of extrapyramidal side effects. Those which are more potent per milligram of dose are less sedating, and more likely to give some extrapyramidal side effects. The newer nonphenothiazine antipsychotics include butyrophenones (Haldol), thioxanthenes (Navane), dibenzodiazepines (Loxitane), and molindone (Moban). They are particularly useful in patients who do not improve on phenothiazines, or who have side effects or allergic reactions which dictate a change of medication.

One medication should be used at a time; polypharmacy is not generally helpful in chemotherapy of schizophrenia. The medication chosen should be given in adequate dosage for a long enough time to have a full effect. Since these medications have a half-life of over 24 hours, a single daily dose can be prescribed rather than the divided dosages necessary for shorter-acting drugs. Antipsychotic effects may occur within a few days, or may not become evident for several weeks. Dosages can be increased at three-day intervals, until the desired effect appears.

Psychotherapy

Psychotherapy is another essential aspect of treatment of schizo-

Continued on page 956

Continued from page 950

phrenic patients. A personal relationship between physician and patient, and the resultant issues of trust, responsibility, and influence, are of critical importance. While psychotherapy alone rarely is sufficient as a treatment for schizophrenia, the planned use of a human relationship can make a significant difference in the way a patient responds to the other components of the treatment plan.

Several purposes are served by the use of psychotherapy in schizophrenia.

1. A model for effective, clear communication with another person can be established and experienced.

2. When rapport and a degree of trust have been established, the therapist is in a position to assist the patient to improve his ability to test reality; this activity is best done in a fashion that encourages the patient to consider nonpsychotic interpretations of his experiences rather than one in which the therapist imposes his views on the patient.

3. The patient can receive necessary emotional support and encouragement.

4. Introspective patients can review their experiences in the postpsychotic phase of illness, to better understand and integrate their recent psychosis in the context of the rest of their lives.

5. Also in the postpsychotic phase, patients with depression can receive support and gain some comfort.

6. After a psychosis, patient and physician can examine the issues and conflicts that may have contributed to the development of a schizophrenic psychosis, with the

aim of lessening the patient's vulnerability for another later psychosis. For example, a young woman who had had two brief but severe schizophrenic psychotic episodes, both after romantic disappointments, was able to learn how she had picked men who would not carry out their end of the relationship.

In beginning psychotherapy the establishment of a trusting relationship is always paramount. This may be particularly difficult with a schizophrenic patient who is fearful, suspicious, and antagonistic. Nonetheless, the therapist can do several things that increase the opportunity for his patient to develop trust. Being open and straightforward is the most helpful attitude, since the patient can sense that he is being dealt with as an adult with rights and responsibilities. The therapist who is sincere, who explains things to his patient, and who lets the patient know what his plans for treatment are will find that the patient appreciates and responds to this respectful attitude. When sessions with other family members are held, the patient should be present whenever feasible. This can reduce the likelihood that he will feel the therapist and his family are doing things behind his back.

A similar flexibility and willingness to place the patient's interests foremost is a sound guideline for any decision that may arise in psychotherapy. The patient who feels he is being treated as an adult by a physician who appeals to the intact and healthy part of his personality will often respond by taking appropriate control of some of his previously disorganized behav-

Continued on page 958

For UTI in their sexually active years...

Macrochantin[®] (nitrofurantoin macrocrystals)

Capsules: 25 mg, 50 mg, 100 mg

INDICATIONS: Macrochantin is indicated for the treatment of urinary tract infections when due to susceptible strains of *Escherichia coli*, enterococci *Staphylococcus aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses), and certain susceptible strains of *Klebsiella* species, *Enterobacter* species, and *Proteus* species.

NOTE: Specimens for culture and susceptibility testing should be obtained prior to and during drug administration.

CONTRAINDICATIONS: Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 40 ml per minute) are contraindications to therapy with this drug. Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of the drug. For the same reason, this drug is much less effective under these circumstances.

The drug is contraindicated in pregnant patients at term as well as in infants under one month of age because of the possibility of hemolytic anemia due to immature enzyme systems (glutathione instability).

The drug is also contraindicated in those patients with known hypersensitivity to Macrochantin, Furadantin[®] (nitrofurantoin), and other nitrofurantoin preparations.

WARNINGS: Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin products. If these reactions occur, the drug should be withdrawn and appropriate measures should be taken.

An insidious onset of pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) in patients on long-term therapy warrants close monitoring of these patients.

There have been isolated reports giving pulmonary reactions as a contributing cause of death. (See Hypersensitivity reactions.)

Cases of hemolytic anemia of the primaquine sensitivity type have been induced by Macrochantin. The hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Negroes and a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Any sign of hemolysis is an indication to discontinue the drug. Hemolysis ceases when the drug is withdrawn.

Pseudomonas is the organism most commonly implicated in superinfections in patients treated with Macrochantin.

PRECAUTIONS: Peripheral neuropathy may occur with Macrochantin therapy; this may become severe or irreversible. Fatalities have been reported. Predisposing conditions such as renal impairment (creatinine clearance under 40 ml per minute), anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrences.

Usage in Pregnancy: The safety of Macrochantin during pregnancy and lactation has not been established. Use of this drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

ADVERSE REACTIONS: Gastrointestinal reactions: Anorexia, nausea and emesis are the most frequent reactions; abdominal pain and diarrhea occur less frequently. These dose-related toxicity reactions can be minimized by reduction of dosage, especially in the female patient. Hepatitis occurs rarely.

Hypersensitivity reactions: Pulmonary sensitivity reactions may occur, which can be acute, subacute, or chronic.

Acute reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution may be dramatic.

In subacute reactions, fever and eosinophilia are observed less often. Recovery is somewhat slower, perhaps as long as several months. If the symptoms are not recognized as being drug related and nitrofurantoin is not withdrawn, symptoms may become more severe.

Chronic pulmonary reactions are more likely to occur in patients who have been on continuous nitrofurantoin therapy for six months or longer. The insidious onset of malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations. Roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations. Fever is rarely prominent.

The severity of these chronic pulmonary reactions and the degree of their resolution appear to be related to the duration of therapy after the first clinical signs appear. Pulmonary function may be permanently impaired even after cessation of nitrofurantoin therapy. This risk is greater when pulmonary reactions are not recognized early.

Dermatologic reactions: Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

Other sensitivity reactions: Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

Hematologic reactions: Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

Neurological reactions: Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

Miscellaneous reactions: Transient alopecia. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

References: 1. Center for Disease Control: *National Nosocomial Infections Study Report*, Annual Summary 1976, issued February 1978. Washington, DC, U.S. Department of Health, Education, and Welfare, p. 8. 2. Cooper J. et al.: Diagnostic and chemoprophylactic importance of perineal microbial carriage, in Siegenthaler W, Luthy R (eds): *Current Chemotherapy*. Washington, DC, American Society for Microbiology, 1978, vol 1, pp 199-200. 3. Buckley RM, McGuckin M, MacGregor RR: Urine bacterial counts after sexual intercourse. *N Engl J Med* 298:321-324, 1978. 4. PMR Bacteriologic Report, Summer Series, 1978; a national bacteriologic monitoring service for 200 acute-care hospitals of 100 beds or more.

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Manati, Puerto Rico 00701

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EMD-9048

Continued from page 956

ior. Most patients can cooperate to a large degree even in a decision such as entering a psychiatric hospital.

In summary, while medications are usually indispensable in treating the psychosis per se, psychotherapy involves treating the patient as a whole person, discovering and fostering the patient's own abilities to control his behavior and to resume competent social functioning. The human context of the patient-physician relationship is important to the patient, for in this collaborative effort he will be learning the necessary tool of clear communication with another person.

Working with the family remains an important consideration in treatment of schizophrenic patients, also.

The patient's family is often a potential and necessary ally. Families can be extremely helpful in carrying out diagnostic evaluation and treatment; they can provide information the patient may be unable to give, and a session with all the family can often demonstrate to the physician much about the ways the family deals with problems and stress. He can then counsel the family on using certain approaches to the patient and avoiding other behavior that places undue pressures or demands on the patient.

In addition, if the patient is out of the hospital for most of his treatment, the family can help supervise his taking medication, getting to clinic or office appointments, and other necessary treatment activities. If the patient is hospitalized, close planning among the hospital staff, the patient, his

family, and the people who will be responsible for afterhospital care is essential to provide a smooth transition back to home and the community.

Social Therapy

Social therapy is the term applied to treatment approaches that affect social functioning and behavior of patients. These approaches include inpatient hospital care, aftercare programs, and vocational/educational rehabilitation. All of these treatment modalities have some place in the planning of each patient's treatment; they should be applied with the same deliberate care that one uses in prescribing a particular dose of a certain medication at a certain point in an illness. Like medications, social therapies can be efficacious when used as indicated, and like medications social therapies can have undesirable effects when used indiscriminately.

Hospitalization is an important tool in psychiatric treatment. Intensive supervision can literally enable a patient to survive a suicidal crisis or a period of irrational excitement and overactivity. Planned therapeutic programs during a hospital stay can allow a patient to discover his abilities and assets, and to find ways to use them to lead a more stable life. The shelter or asylum provided in any hospital stay can be an opportunity to take stock, to sort out the various forces and demands in one's life, and to make plans to deal effectively with these stresses rather than becoming

Continued on page 964

PERCOCET-5[®] (Tablets)

Brief Summary of Prescribing Information

DESCRIPTION Each tablet of PERCOCET[®]-5 contains 5 mg oxycodone hydrochloride (WARNING: May be habit forming), 325 mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET[®]-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET[®]-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET[®]-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET[®]-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET[®]-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET[®]-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET[®]-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET[®]-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET[®]-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET[®]-5 may be additive with that of other CNS depressants. See WARNINGS. 6085 5S

DEA Order Form Required.

PERCOCET[®] is a U.S. registered trademark of Endo Inc.

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Manati, Puerto Rico 00701
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ENDO-644E 579

Continued from page 958

overwhelmed by them. Living together with other people in a unit of an inpatient service can be a new experience in sharing and developing human relationships, something that schizophrenic patients often have great difficulty doing on their own.

There are several relative indications for hospitalizing a patient, and a few conditions for which hospitalization is absolutely necessary. The absolute indications include severe suicidal risk, profound withdrawal or excitement in a catatonic state, and extreme disorganization that makes it impossible for a patient to cooperate in controlling his own behavior. In situations less severe than these, the decision for hospitalization is made by balancing the benefits of hospital care; the patient's relative ability to cooperate and participate in his own treatment; the available alternatives such as daily office or clinic visits, partial hospital services (day hospital), the ability of family to help supervise the patient; and the possible risks of hospital care (eg, increased inappropriate dependency; loss of social role, such as job).

A patient who requires close supervision because of a rapidly changing clinical state, who presents a problem in diagnosis, or who requires large doses of a medication not taken before may receive better care if he is hospitalized during the initial stage of treatment. Likewise, the patient who has a disrupted life with little or no family or other social support may require hospitalization for effective treatment.

Chronically ill schizophrenic patients may be hospitalized briefly

and periodically when their families need a respite from the full responsibility of caring for them. These respite hospitalizations can be an opportunity for patient, family, and physician to reevaluate the total approach to long-term treatment. Such a hospitalization is generally time-limited, and discharge is planned from the day of admission.

Facilities for inpatient psychiatric care vary from community to community. The several types are psychiatric beds or units in a general hospital, private psychiatric hospitals, and public (state or county) psychiatric hospitals. General hospital psychiatric services have increased greatly in the last 20 years, and such inpatient units can offer intensive diagnostic and therapeutic care during a short-term hospitalization. Care in such general hospital units is usually covered by Blue Cross and other medical insurance policies. Another advantage of the general hospital psychiatric unit is that it is usually close to the patient's home and family, so a smooth transition can be made at discharge.

Private psychiatric hospitals offer long-term care, generally, and can provide intensive therapy for patients who may require several months of inpatient care to regain function. They often have specialized units or specific psychiatrists who have concentrated on doing therapy with difficult schizophrenic patients.

State and county public psychiatric hospitals offer both acute and chronic care. For a patient who has no medical insurance, a brief hospitalization in a public hospital may be the only choice if he is too ill for outpatient care. State hospitals

Continued on page 966

FOR DEEP INTRAMUSCULAR INJECTION ONLY.

Indications: In treatment of infections due to penicillin G-sensitive microorganisms susceptible to the low and very prolonged serum levels common to this dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and clinical response.

The following infections usually respond to adequate dosage of IM penicillin G benzathine. **Streptococcal infections** (Group A—without bacteremia). Mild to moderate upper respiratory infections (e.g., pharyngitis).

Veneral infections—Syphilis, yaws, bejel, and pinta.

Medical conditions in which penicillin G benzathine therapy is indicated as prophylaxis:

Rheumatic fever and/or chorea—Prophylaxis with penicillin G benzathine has proven effective in preventing recurrence of these conditions. It has also been used as followup prophylactic therapy for rheumatic heart disease and acute glomerulonephritis.

Contraindications: Previous hypersensitivity reaction to any penicillin.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported. Anaphylaxis is more frequent following parenteral therapy but has occurred with oral penicillins. These reactions are more apt to occur in individuals with history of sensitivity to multiple allergens. Severe hypersensitivity reactions with cephalosporins have been well documented in patients with history of penicillin hypersensitivity. Before penicillin therapy, carefully inquire into previous hypersensitivity to penicillins, cephalosporins and other allergens. If allergic reaction occurs, discontinue drug and treat with usual agents, e.g., pressor amines, antihistamines and corticosteroids.

Precautions: Use cautiously in individuals with histories of significant allergies and/or asthma.

Carefully avoid intravenous or intraarterial use, or injection into or near major peripheral nerves or blood vessels, since such injection may produce neurovascular damage.

In streptococcal infections, therapy must be sufficient to eliminate the organism, otherwise the sequelae of streptococcal disease may occur. Take cultures following completion of treatment to determine whether streptococci have been eradicated.

Prolonged use of antibiotics may promote overgrowth of non-susceptible organisms including fungi. Take appropriate measures if superinfection occurs.

Adverse Reactions: Hypersensitivity reactions reported are skin eruptions (maculopapular to exfoliative dermatitis), urticaria and other serum sickness-like reactions, laryngeal edema and anaphylaxis. Fever and eosinophilia may frequently be only reaction observed. Hemolytic anemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are infrequent and usually associated with high parenteral doses.

As with other antisyphilitics, Jarisch-Herxheimer reaction has been reported.

Composition: (units penicillin G benzathine as active ingredient in aqueous suspension): 300,000 units per ml—10-ml multi-dose vial. Each ml also contains sodium citrate buffer approximately 6 mg lecithin, 3 mg povidone, 1 mg carboxymethylcellulose, 0.5 mg sorbitan monopalmitate, 0.5 mg polyoxyethylene sorbitan monopalmitate, 1.2 mg methylparaben and 0.14 mg propylparaben.

600,000 units in 1-ml TUBEX® (sterile cartridge-needle unit) Wyeth, packages of 10.

900,000 units, 1.5-ml fill in 2-ml TUBEX, packages of 10.

1,200,000 units in 2-ml TUBEX, packages of 10, and in 2-ml single-dose disposable syringe, packages of 10.

2,400,000 units in 4-ml single-dose disposable syringe, packages of 10.

Each TUBEX or disposable syringe also contains sodium citrate buffer and, as w/v, approximately 0.5% lecithin, 0.6% carboxymethylcellulose, 0.6% povidone, 0.1% methylparaben and 0.01% propylparaben.

INJECTION

BICILLIN® LA**(STERILE PENICILLIN G BENZATHINE SUSPENSION)**

Wyeth Laboratories Philadelphia, Pa. 19101

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Continued from page 964

have changed over the years also, and many patients are discharged within a few weeks, to return to community-based outpatient care. The patient who has not responded to therapy, and who cannot live independently or with family in the community, may require indefinitely long inpatient care. Here the state hospital may be the place of choice for those with limited or exhausted financial means.

Most patients will agree to voluntary hospital care, but some will refuse or be unable to cooperate. In these instances, the physician must decide if he will begin commitment procedures to require the patient to enter a hospital involuntarily. Different states have different regulations about involuntary admission; a usual situation for which involuntary admission is allowable is the patient who, because of his psychiatric illness, presents an immediate danger to himself (suicide; risk-taking, such as running into traffic) or to others (threats of assault or homicide). In most states two physicians examine the patient, and if they both find that he is psychiatrically ill and presents a danger, they sign the appropriate papers. These papers are then presented to the receiving hospital, by family or by the court system. Involuntarily admitted patients are examined, treated, and subsequently their situation is reviewed to determine if they still require involuntary hospitalization. Virtually all public mental hospitals receive involuntary patients, and many private psychiatric hospitals also do so.

After hospitalization some patients return to their homes, while others are referred to a half-

way house for further therapy in a setting where they can take some steps toward independence, within a structured and planned environment. Halfway houses, in which patients generally stay three to ten months, are located within communities, and patients living there often take part-time or full-time jobs, or return to school. In these facilities patients can further develop social abilities and at the same time keep a distance from some of the family tensions and demands that may have exacerbated their illness.

Whether a patient goes home, or to a halfway house, or lives on his own after hospitalization, a well-planned aftercare program is an essential step in ensuring maximum opportunity for recovery. This can be done within the same institution that provided the inpatient care, or by another outpatient clinic, or by a private practitioner with the collaboration of social or rehabilitation services. A particularly useful model of aftercare is described by Donlon and Rada.⁶ It includes group therapy of a supportive nature, medications, socialization groups in which patients can further develop their social skills, and aggressive follow-up for any patient who misses an appointment. Patients become loyal to such an aftercare program, and can readily turn to it for as much as they may need in any stage of their recovery. At the same time, a good aftercare program will place definite demands upon its patients, challenging them in a supportive fashion to make the most of their lives by seeking jobs or education.

Vocational and educational rehabilitation services can help many

Continued on page 970

Sanorex® (mazindol)Ⓒ

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given a pressor amine agent (e.g., levaterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: An increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses.

Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. **Cardiovascular:** Palpitation, tachycardia. **Central Nervous System:** Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. **Gastrointestinal:** Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. **Skin:** Rash, excessive sweating, clamminess. **Endocrine:** Impotence, changes in libido have rarely been observed. **Eye:** Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: Usual dosage is 1 mg, three times daily, one hour before meals, or 2 mg, once daily, one hour before lunch. Use lowest effective dose, which can be determined by starting therapy at 1 mg, once a day and adjusting to the need and response of the patient. Should GI discomfort occur, mazindol may be taken with meals.

Overdosage: There are no data as yet on acute overdosage with mazindol in humans. Manifestations of acute overdosage with amphetamines and related substances include restlessness, tremor, rapid respiration, dizziness. Fatigue and depression may follow the stimulatory phase of overdosage. Cardiovascular effects include tachycardia, hypertension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting and abdominal cramps. While similar manifestations of overdosage may be seen with mazindol, their exact nature have yet to be determined. The management of acute intoxication is largely symptomatic. Data are not available on the treatment of acute intoxication with mazindol by hemodialysis or peritoneal dialysis, but the substance is poorly soluble except at very acid pH.

How Supplied: Tablets, 1 mg. and 2 mg., in packages of 100. Before prescribing or administering, see package circular for Prescribing Information

Continued from page 966

recovering patients to return to former occupations or to choose new fields better suited to their abilities and their vulnerabilities. These services, usually run by state or local departments of education, can also provide some financial support for patients in the transition from dependent hospital patient to productive member of the community. A further note here: a trend in state laws is to forbid employers to refuse a job to someone merely because the person has been a mental patient. Therefore, when the general job market is good, the prospects of a patient finding a job may also be good; every effort should be made to help a recovering patient gain the necessary skills to obtain employment.

Other therapies should be briefly mentioned. Electroconvulsive therapy, used mostly for psychotic depressions, also may provide quicker recovery than would medications for a schizophrenic patient in a catatonic withdrawal. Megavitamin therapy, with high doses of nicotinic acid and other vitamins, has not been shown to offer any significant help for schizophrenic patients; in fact, most reports of the treatment include large groups of patients who have been given phenothiazines in addition to the vitamins, and results are equivocal at best.

In summary then, there are effective therapeutic approaches for patients with schizophrenic illnesses. It is a matter of finding the combination of approaches that best fits the individual patient. Antipsychotic medication, some form of psychotherapy, and a plan to improve social functioning are all

essential components. Most patients can gain significant improvement, and many will recover completely. Lehmann states that of patients hospitalized for an acute schizophrenic episode, 60 percent will show good social recovery in a five-year follow-up, 30 percent will have some handicaps, and only ten percent will be in a hospital.⁹

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SYNEMOL®

(FLUOCINOLONE ACETONIDE)
CREAM 0.025%

Description SYNEMOL (fluocinolone acetonide) has the chemical name 6 α , 9 α -difluoro-16 α -hydroxyprednisolone-16, 17-acetonide.

The cream contains fluocinolone acetonide 0.25 mg./g. in a water-washable aqueous emollient base of stearyl alcohol, cetyl alcohol, mineral oil, propylene glycol, sorbitan monostearate, polysorbate 60, purified water and citric acid.

Indications Inflammatory manifestations of corticosteroid-responsive dermatoses.

Contraindications Topical steroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Precautions If irritation develops, discontinue the product and institute appropriate therapy.

In the presence of an infection institute the use of an appropriate antifungal or antibacterial agent. If a favorable response does not occur promptly, discontinue the corticosteroid until the infection has been adequately controlled.

If extensive areas are treated or if occlusive technique is used, there will be increased systemic absorption of the corticosteroid and suitable precautions should be taken, particularly in children and infants.

The safety of topical steroids in pregnant women has not absolutely been established. In laboratory animals, increases in incidences of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids, in some cases at rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients, in large amounts or for prolonged periods of time.

SYNEMOL® (fluocinolone acetonide) cream is not for ophthalmic use.

Adverse Reactions Local adverse reactions reported with topical corticosteroids: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, miliaria.

How Supplied
SYNEMOL® (fluocinolone acetonide)
Cream 0.025% — 15, 30 and 60 g. tubes.



Syntex Laboratories, Inc.
Palo Alto, California 94304