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ADVERSE REACTIONS TO DRUGS

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THE NUMBER of therapeutic agents is continually growing. Unfortunately, some of the most useful drugs present troublesome problems, and drugs of molecular structure that did not exist a short time ago are causing an increase in the rate of undesired reactions, ranging from minor to fatal.

An undesired reaction is a phenomenon clearly distinct from the usual pharmacological effect of the drug prescribed. A true adverse reaction to a drug is the result of individual idiosyncrasy. The application of penicillin, topically or by aerosol, for example, may provoke an undesired reaction. We know that there must be a specific immune response by the recipient before such a reaction can develop. The reason is, therefore, due to an idiosyncrasy on the part of the patient.

The writer's review of one thousand patients who were admitted to three different hospitals disclosed 68 adverse reactions. Some of the unwanted effects may have been due to the pharmacologic effects of either a normal or excessive dosage.

Classification of Reactions

ALLERGIC. Adverse reactions to drugs are classified as allergic or toxic. The classification is convenient because a number of the toxic reactions, such as widespread vasculitis, may have an allergenic mechanism. An allergy to a drug may assume the same form as an allergy due to other agents. The sites of predilection may differ, along with either the known or unidentified allergenic properties of the drug administered. Urticaria, dermatitis, serum sickness, asthma, and anaphylaxis are among the allergic reactions to drugs.

TOXIC. Toxic reactions include atypical eruptions, exfoliative dermatitis, blood dyscrasia, and specific organ damage (hepatitis, nephrotoxic reactions, and polyarteritis). These syndromes usually are not regarded as allergic phenomena, although in many instances they are a result of

hypersensitivity. A toxic effect occurs in direct relation to the total amount of the drug in the body. The effect occurs if the blood threshold level is exceeded; the result may be due to overdosage or to the cumulative effect of the drug in the body. Relative overdosage occurs under certain conditions, i.e., a patient who suffers from renal tuberculosis often tolerates only small doses of streptomycin. Potassium may prove dangerous in uremic patients, because of the inability of the kidneys to secrete properly; hexamethonium chloride (Hexamethonium Chloride, Methium Chloride), may also produce a severe and prolonged reaction in these patients. Another good example of relative overdosage is the sensitization of patients to the effect of digitalis by a low serum potassium (elevated calcium, depressed potassium). Electrocardiographic changes of digitalis poisoning may appear if the serum potassium of a digitalized patient falls; these symptoms often respond to the administration of potassium.

At one time, it was almost certain that the presence of a papular rash was due to the use of iodides, bromides, or Fowler's solution. This is no longer the case. The number of compounds used by the modern physician, in addition to those present in proprietary preparations or as food additives, is so great that only a careful history makes identification of a causative agent possible. If an eruption appears after a drug has been used for some time, disappears on discontinuation, and

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returns when the patient takes the drug again, the antigenic nature of the drug may be assumed.

Drug Intolerance

Intolerance to a drug is a lowered threshold to the normal pharmacologic reaction to the drug. It results from variation in rate of absorption, metabolism, or excretion, or from susceptibility to the drug administered. Unusual effects of morphine, for example, are weakness and depression, delirium, nausea and vomiting, excitement, convulsions, insomnia, urticaria, and dermatitis with itching and sneezing, instead of relaxation. In some patients morphine intolerance or idiosyncrasy, even to a very small dose, may cause deep sleep. In others, a very large dose of morphine may cause only a slight adverse effect. Old persons and children are especially susceptible to morphine.

A secondary effect of a drug is the indirect result of its primary action. The secondary effect has assumed extreme importance since the introduction of antibiotics, and may result from the direct pharmacologic action of the drug administered. The secondary effect may also develop from the intended effect of the drug. The broad spectrum antibiotics may produce the following secondary effects: (1) anorectal syndrome; (2) *Candida albicans* infections, and, on occasion, vitamin deficiency; (3) gram-negative bacteremia; (4) reactions to released products of killed microorganisms; (5) penicillin resistant, coagulase-positive staphylococcus infections, and (6) photodynamic reactions to sunlight on exposed parts of the body, demethylchlortetracycline hydrochloride and nystatin (Declostatin), and demethylchlortetracycline (Declomycin).

Side Effects

The undesired effect which follows the administration of some drugs is due to the normal pharmacologic effect of the drug. As a result, the dose administered has to be graduated if the desired pharmacologic actions are to be obtained with a minimum of undesired side effects. The hypnotic effect of many antihistamine drugs, for example, limits their dosage. Some drugs act as histamine-releasing agents. As a result, the direct action of the drug is overshadowed by the histaminic effect. Megaloblastic anemia has been reported in epileptic patients treated with phenindone (Danilone, Hedulin), and primidone (Mysoline).

✓ **ALLERGIC.** There is evidence that blood dyscrasias following the administration of a drug

have an allergenic basis. Initially, a drug may be administered and not produce harm. When the drug is readministered, however, the sensitized patient may develop agranulocytosis, serum sickness, and other ill effects. It is also known that even a small dose of the same drug will produce the dyscrasias.

NONSPECIFIC. Side effects that cannot be explained in the pharmacologic terms are classified as nonspecific. Many untoward reactions have been observed following the administration of tranquilizers, the so-called phenothiazine derivatives; the untoward reactions of urticaria, generalized pruritis, jaundice, hepatitis, weight gain, gynecomastia, lactation, blurring of vision, and agranulocytosis are well recognized.

EXTRAPYRAMIDAL. Some potent phenothiazine derivatives possess lesser sedative properties but a greater propensity to cause neurologic side effects, now known as extrapyramidal reactions. These neurologic reactions, which include dyskinesia, dystonia, akinesia (motor restlessness), ataxia, loss of libido, and parkinsonism differ in type and incidence, and they depend upon the phenothiazine derivative administered. These reactions occur most frequently with agents in the perphenazine (Trilafon), trifluoperazine (Stelazine), and prochlorperazine (Compazine) groups. Convulsive seizures following the administration of promazine hydrochloride (Sparine) have been reported in the literature. The physician, and particularly the allergist, is often confounded by the side effects that occur following the administration of some drugs. Jaundice following the application of resorcin ointment, and other adverse reactions following the use of beverages containing artificial flavoring and coloring agents are common. Allergic individuals, exposed previously to these agents, may experience bizarre reactions.

✓ Idiosyncrasy

Terms often used synonymously are hypersensitivity and idiosyncrasy. European physicians prefer the term idiosyncrasy to hypersensitivity, while in American medical literature, the terms allergy and hypersensitivity are often used synonymously to describe the same entity. In describing a reaction, one must carefully differentiate between a reaction which is artificially induced or acquired and one which occurs naturally and is directly related to heredity. The best example of a true idiosyncrasy is the frequent occurrence of a hemolytic anemia in American Negroes who have been treated with Primaquine, an anti-

malarial drug. Scientists have demonstrated that the red blood cells of Negroes are deficient in a specific enzyme, and therefore, their reaction to Primaquine is probably due to an inborn idiosyncrasy to the drug.

Hypersensitivity

Hypersensitivity is a reaction in which the symptoms have been conditioned by previous exposure plus sensitization, or cross-sensitization, to a particular drug. Allergists feel that reactions of this type are mediated by an antigen-antibody reaction. These drugs may be grouped under the terms hypersensitivity or allergic reactions to a drug or drugs. There is an overlap between groups of drugs, and it is almost impossible to place every known drug with its molecular structure under a particular heading or classification.

Allergic Reaction

The allergic reaction to a drug may be sudden or delayed. There are two types of reactions: (1) anaphylactic shock, and (2) serum sickness.

ANAPHYLACTIC SHOCK. The onset of anaphylactic shock is immediate. The patient usually turns pale and has sensations of tingling or burning accompanied by severe pain in the chest, a feeling of constriction, and impending death. Dyspnea and cyanosis are often present. A rapid fall in blood pressure and loss of consciousness take place. A dose of 1:1,000 epinephrine hydrochloride must be administered immediately and repeatedly. It is the drug of choice; otherwise, death may follow in a few minutes. After epinephrine is administered initially, other drugs may be used.

SERUM SICKNESS. Serum sickness is manifested by fever, joint pains, skin eruptions, and lymphadenopathy. This syndrome usually appears within two weeks after the injection of a foreign serum (sera of equine origin). Statistics reveal that the incidence of serum sickness is always high in patients who are given the causative agent in dosages of 100 ml. or more. The most severe reactions occur in sensitive individuals who receive serum by intravenous or intraspinal routes. Patients who develop serum sickness often have a history of asthma, hay fever, or some other type of allergy. Typical serum sickness usually begins with pruritic skin manifestations. Several days later, mild to severe polyarthritis develops in 50 to 66 percent of the patients. Approximately one patient in three has fever. The anaphylactic shock usually appears immediately after the administration of a foreign serum. The

Table 1

Anaphylactic Kit

- Epinephrine hydrochloride 1:1,000 (parenteral), 1 multiple dose vial.
- 3 sterile 1 ml. ampules 1:1,000 epinephrine hydrochloride.
- 3 disposable 1 ml. tuberculin syringes with needles.
- 2 sterile, 2 ml. syringes.
- 2 hypodermic needles, 23 gauge, 5/8 inch.
- 2 hypodermic needles, 22 gauge, 1 inch.
- 2 hypodermic needles, 22 gauge, 4 inch.
- 2 sterile ampules aminophyllin U.S.P., 4 Gr.
- 1 sterile ampule, 250 ml., 5 percent glucose in distilled water.
- 1 intravenous set.
- 1 sterile vial chlorpheniramine maleate (Chlor-Trimeton Maleate), 100 mg. per ml.
- 1 sterile vial chlorpheniramine maleate, 10 mg. per ml.
- 1 sterile vial injectable diphenhydramine hydrochloride (Benadryl), 10 mg. per ml.
- 1 sterile ampule methylprednisolone sodium succinate (Solu-Medrol), 40 mg. per ml.
- 1 sterile vial injectable prednisolone 21-phosphate (Hydeltrasol Injection), 20 mg. per ml.
- 1 sterile vial injectable dexamethasone (Decadron), 4 mg. per ml.
- 1 scalpel, 2 hemostats, 1 ampule of catgut with needle, alcohol, gauze sponges, tongue depressor, 1 syringe, 20 ml., 1 tracheotomy set.
- 1 sterile needle, 14 gauge, for insertion below glottis in tracheal edema.
- 1 tourniquet.
- 1 sterile vial meperidine hydrochloride (Demerol Hydrochloride), 50 mg. per ml.
- Small oxygen tank and mask.
- Levarterenol bitartrate (Levophed Bitartrate).

two types of reactions described above can also result from the administration of many drugs.

We know that the skin manifestations of sensitivity are due to antigen-antibody union between proteins and hapten antibody union between drugs that do not contain a protein complement. Allergic reactions are the manifestations of the response of the tissues to antigen-antibody reaction.

In addition to allergic reactions, antibiotics often exert toxic effects. Penicillin administered in an excessive dose intrathecally will damage the brain. Similarly, streptomycin U.S.P. will damage the eighth nerve; bacitracin (Bacitracin, Baciguent), and polymyxin B preparations (Polymixin B Sulfate), the kidney, and excessive doses of the tetracyclines, the liver. I shall discuss only those reactions normally seen and known to result from sensitization due to previous exposure to the antibiotic. Two main types

of sensitivity reactions are very similar to those produced by foreign protein, such as that present in horse serum: (1) anaphylactic shock, and (2) serum sickness.

A third form of sensitization is due to an alteration in the reactivity of certain tissue which results in degeneration or inflammatory changes if the antigen is applied again, i.e., marrow aplasia produced by chloramphenicol (Chloromycetin). Evidence that blood dyscrasias following drug administration have an allergic basis has been cited in numerous articles in medical literature. Initially, the drug did no harm. When the drug was administered the second time, the sensitized patient developed agranulocytosis. When readministered, a very minute dose of the same drug will again produce the dyscrasia.

✓ Since only a very small percentage of patients have reactions to particular drugs, this indicates idiosyncrasy of some kind. Research over the past twenty-five years has pointed to the aniline derivatives. It is thought that these derivatives are most likely to affect the bone marrow. Cross-sensitization to compounds which yield quinone metabolites has been demonstrated, and suspicion has been cast on the so-called nitrobenzene group of drugs. We cannot state that any one molecule more than another is likely to produce a drug dyscrasia or to sensitize. Agranulocytosis has occurred after the administration of aminopyrine (Pyramidon), the hydantoins, various gold salts, arsenicals, phenylbutazone (Butazolidin), and the thiouracils.

Acute Allergic Emergencies

ANAPHYLACTIC KIT. Since whatever is to be done has to be done quickly in the management of acute allergic emergencies, the necessary supplies must always be readily at hand. An emergency tray should be set up and ready in every physician's office (Table 1). It should be inspected once a week to see that everything is in order for immediate use.

MANAGEMENT. The following steps should be taken in the management of acute allergic emergencies: Place a tourniquet between the site of injection and the body. Treat the anaphylactic shock first, and then initiate steps to reduce localized edema in the larynx and bronchi.

Wet a 2 ml. syringe with 1:1,000 epinephrine hydrochloride; withdraw blood into the syringe, where it will mix with the epinephrine hydrochloride, and reinject intravenously, slowly. Inject 0.5 ml. of 1:1,000 epinephrine hydrochloride

intramuscularly, of which 0.2 ml. may be injected into the site of an antigen injection, if that is what caused the emergency. If necessary, give another 0.5 ml. of 1:1,000 epinephrine hydrochloride intramuscularly minutes later, and if improvement is still not apparent, inject 0.2 ml. of 1:1,000 epinephrine hydrochloride in 2 ml. dexamethasone (Decadron, Deronil, Gammacorten, Hexadrol) containing 20 mg. per ml. intravenously, slowly.

Place the patient in the head-low position and keep him warm. Should the patient be an asthmatic with complications of dyspnea, respiratory difficulties, and wheezing, give him $3\frac{3}{4}$ to 4 Gr. aminophyllin U.S.P. intravenously. If the patient is cyanotic, administer oxygen, and administer artificial respiration immediately if respiratory movements become poor or cease. If the patient is in the hospital, the administration of oxygen with intermittent pressure apparatus may be helpful. If necessary, give 1:1,000 epinephrine hydrochloride intracardially.

If laryngeal edema occurs, perform an emergency tracheotomy; if necessary, an antihistamine, such as 50 mg. of diphenhydramine hydrochloride (Benadryl) or 10 mg. of chlorpheniramine maleate (Chlor-Trimeton Maleate) may be given intramuscularly or intravenously.

If the patient remains in profound and continued shock, as shown primarily by persistent low blood pressure, add 2 ml. or 1:1,000 epinephrine hydrochloride or 4 ml. of levarterenol bitartrate (Levophed Bitartrate), plus 20 to 40 units of lypholized corticotropin U.S.P. (ACTH) to 1,000 ml. of 5 percent glucose in saline solution or distilled water and adjust the rate of flow intravenously to maintain blood pressure.

Antibiotic Sensitization

PENICILLIN. Shortly after the inception of penicillin therapy, it was learned that this antibiotic combines with plasma protein and that this combining power is exclusively with the albumin fraction. The proportion bound differs with the form of penicillin. It is greatest with penicillin K, and because of this, penicillin K is considered therapeutically inferior and has fallen into disuse. When we assay penicillin in plasma or serum, protein binding must be taken into account. Since protein binding takes place, penicillin behaves as a haptene. Immunologists and allergists assume that antibody is formed to the penicillin albumin complex. We have all seen the serum sickness-like, delayed, urticarial type of reaction which occurs in penicillin-sensitive patients following its administration (Table 2).

Table 2

Dermatologic Manifestations of Drug Reactions

Reaction	Most Common Offending Drugs
Urticaria	Organ extracts, penicillin, streptomycin, salicylates, sera, food adulterated with coloring, flavoring, and preservative agents of coal tar origin.
Allergic exzematous dermatitis	Sulfonamides, penicillin, mercurials, arsenicals, local anesthetics, quinacrine hydrochloride U.S.P. (Atabrine Hydrochloride), quinine sulfate U.S.P., aniline dyes, arsephenamine.
Fixed eruptions	Barbiturates, phenosulfonphthalein, quinacrine hydrochloride U. S. P., sulfonamides, gold, phenacetin, anti-pyrine.
Erythema multiforme and nodosum-like lesions	Bromides, iodides, salicylates, phenacetin, sulfonamides, penicillin, phenosulfonphthalein.
Purpura	Barbiturates, gold salts, iodides, sulfonamides, arsphenamines.
Exanthematic	Barbiturates, sulfonamides, heavy metals, arsenic, salicylates, foods adulterated with coloring, flavoring, and preservative agents of coal tar origin, penicillin.
Bullous eruptions	Iodides, gold, salicylates, sulfonamides, phenosulfonphthalein.
Exfoliative dermatitis	Arsenicals, barbiturates, gold salts, mercurials, quina-crine, belladonna.

I do not think that there is a clinical distinction between the reaction due to penicillin itself and that due to drugs. Nurses, physicians, manufacturers, medical staffs, and pharmacists who handle penicillin are prone to this type of sensitization, which can occur through contact or by inhalation.

Statistics reveal that penicillin is now the most common cause of anaphylactic shock. This fact should always be considered whenever penicillin is administered. The use of penicillin in minor conditions is contraindicated. A search of vital statistics for 1962 reveal the following causes of death from anaphylactic reactions: penicillin and other antibiotics, 223; aspirin, 31; sera, 39; sensitized subjects stung by bees, hornets, wasps, yellow jackets, fire ants, scorpions, and other unspecified insects, 37; venomous snakes, 17. These statistics indicate that penicillin should be used with caution. Before administering penicillin to any patient, the physician should question the patient about any previous allergic manifestations, such as asthma, hay fever, perennial vasomotor rhinitis, infantile eczema, neurodermatitis, clinical reactions to berries, sea foods, and other foods. Asthmatics are particularly prone to penicillin sensitization. Care should be taken to prevent the intravascular injection of penicillin through the inadvertent penetration of a small venule or arteriole.

STREPTOMYCIN U.S.P. Streptomycin is a rare cause of shock-like reaction. It is, however, a common cause of the urticarial type of reaction which, at times, is accompanied by fever (Table 3). Nurses and physicians are often sensitized to streptomycin by contact. Sensitization occurs when the droplets of concentrated solution are scattered during the process of expelling air from a syringe. The expelled droplets contaminate the skin of the hands, face, and eyes. To avoid sensitization to streptomycin, the air in the syringe should be expelled into the vial containing the solution before the needle is withdrawn to prevent back pressure. Remember that the hands and face may also be contaminated if gloves are not worn to take apart the syringe. If the hands become contaminated, wash immediately with warm water and soap.

TETRACYCLINES. Numerous reactions of the urticarial type have been reported. Toxic renal manifestations and excessive sodium excretion are among other reactions, and the tetracyclines must always be administered carefully in the presence of preexisting renal disease. Our choice in this series of drugs is tetracycline hydrochloride (Polycycline, Steclin).

CHLORAMPHENICOL. Anaphylactic and serum-type reactions are almost unknown with chloramphenicol. The marrow aplasia reported has

Table 3

Systemic Diseases Caused by Drugs

<i>Causative Agents</i>	<i>Disease or Syndrome</i>	<i>System</i>
Anesthetics, mercurials, penicillin, procaine amide penicillin, sulfonamides, sera, acetylsalicylic acid, insulin.	Anaphylactic shock, polyarteritis nodosa.	Vascular
Penicillin, aureomycin, meperidine hydrochloride (Demerol), para-amino-salicylic acid, pollen extracts, bacterial vaccines, acetylsalicylic acid, arsenic, belladonna.	Asthma.	Pulmonary
Hydralazine hydrochloride (Apresoline Hydrochloride)	Lupus-like erythematosus.	Collagen
Oxygen in premature infants.	Retrolental fibroplasia.	Metabolic
Chlorpromazine hydrochloride (Thorazine), Thiouracil, methimazole (Tapazole), erythromycin sulfate (Ilosone).	Jaundice, intrahepatic cholestasis, obstruction.	Hepatic
Phenacemide (Phenurone), phenylbutazone (Butazolidin), isonicotinic acid-hydrazone, high protein intake.	Hepatitis, hepatic coma.	Hepatic
Sulfonamides, trimethadione U.S.P. (Tridione), chelating agents, autonomic blocking agents.	Nephroses, acute urinary retention.	Renal
Tranquilizers, particularly trifluoperazine (Stelazine), perphenazine (Trilafon), prochlorperazine (Compazine), reserpine, Rauwolfia serpentina, steroids, streptomycin U.S.P., dihydrostreptomycin preparations.	Convulsive disorders and parkinsonism, psychoses, eighth nerve.	Neurologic
Antithyroid drugs, phenylbutazone, chloramphenicol, amphetamine preparations, trimethadione U.S.P., diphenylhydantoin sodium U.S.P. (Dilantin), pyridostigmin bromide (Mesantoin), hydralazine hydrochloride, tolbutamide (Orinase), chlorpromazine hydrochloride, aminopyrine (Pyramidon).	Hemotoxic reactions.	Hematologic

been regarded as resulting from sensitization by previous or prolonged treatment. If chloramphenicol is administered in large doses, always do adequate blood studies. When blood counts show unusual deviations, such as leukopenia or thrombocytopenia, chloramphenicol U.S.P. should be discontinued. If the count falls below 50 percent, discontinue the drug. Do not administer this drug to premature infants because they do not excrete it.

NOVOBIOCIN SODIUM U.S.P. (ALBAMYCIN SODIUM, CATHOMYCIN SODIUM). Severe skin reactions accompanied by fever are common after administering this drug for seven days. Novobiocin possesses a strong sensitizing capacity because it combines extensively with plasma protein.

ASPIRIN. The most common reaction of sensitivity to aspirin is severe angioneurotic edema about the head, face, palms of the hands, and soles of the feet. Cazort pointed out that it is useless to ask the patient whether or not he has taken aspirin. It is much better to inquire about the recent headache or indisposition and what he may have taken for it. If he took a proprietary remedy, it probably contained aspirin. A woman who has urticaria with her menses is usually

sensitive to aspirin. I shall not dwell on the dangerous reaction to aspirin which develops rapidly, with an ashen or cyanotic color, violent paroxysms of asthma, and which quickly results in death if not treated. The onset of this reaction occurs within two hours after taking aspirin, and most commonly within twenty minutes. The dose may be small, or the patient may be generally known to be clinically sensitive to aspirin. Usually 1:1,000 epinephrine hydrochloride injected subcutaneously, and if necessary, intravenously, is effective in restoring the airway. One or two doses may be enough. Never prescribe aspirin to an asthmatic unless he has taken the drug previously with no ill effect.

POLYMYXIN AND COLISTIN (COLY-MYCIN). Polymyxin B preparations and colistin are used in treatment of infections due to gram-negative bacteria. In using these drugs, one must watch for the overgrowth of nonsusceptible organisms, particularly strains of proteus. One should also watch for neurologic manifestations and parasitiasis.

METHYLLIN, SODIUM OXACILLIN (PROSTAPHILIN), AND POTASSIUM PENICILLIN-152 (SYNGILLIN). In the use of these drugs, watch for skin

rash, pruritis, urticaria, gastrointestinal disturbances (nausea, vomiting, diarrhea), and fever. With sodium oxacillin therapy, a few instances of serum glutamic oxaloacetic transaminase (SGOT) have been observed. The significance of this elevation is unknown. Occasional cases of agranulocytosis have been reported. Perform white blood counts frequently.

DEMETHYLCHLORTETRACYCLINE. Photodynamic reactions to sunlight have been observed. There are also rare anaphylactic reactions.

NITROFURANTOIN (FURADANTIN). In administering nitrofurantoin, watch for erythematous, maculopapular cutaneous eruptions or urticaria, asthmatic symptoms, muscular aches, or jaundice. Cases involving fall of blood pressure have also been reported.

- If a bibliography is desired, one will be sent upon request to the JOURNAL office, 230 State Street, Harrisburg.

- **GENERIC AND TRADE NAMES OF DRUGS.** Aminopyrine—*Pyramidon*; Chloramphenicol U.S.P.—*Chloromy-*

ctin; Chlorpheniramine maleate—*Barclophen, Chlor-Trimeton Maleate, Histadur Dura-Tabs, Teldrin*; Chlorpromazine hydrochloride—*Thorazine*; Colistin—*Colymycin*; Corticotropin U.S.P.—*ACTH*; Demethylchlortetracycline—*Declomycin*; Demethylchlortetracycline hydrochloride and nystatin—*Declostatin*; Dexamethasone—*Decadron, Deronil, Gammacorten, Hexadrol*; Diphenhydramine hydrochloride—*Benadryl*; Diphenhydantion sodium U.S.P.—*Dilantin*; Erythromycin sulfate—*Ilosone*; Hexamethonium chloride—*Hexamethonium Chloride, Methium Chloride*; Hyalalazine hydrochloride—*Apresoline Hydrochloride*; Levarterenol bitartrate—*Levophed Bitartrate*; Meperidine hydrochloride—*Demerol Hydrochloride*; Methimazole—*Tapazole*; Methylprednisolone sodium succinate—*Solu-Medrol*; Novobiocin sodium U.S.P.—*Albamycin Sodium, Cathomycin Sodium*; Perphenazine—*Trilafon*; Phenacemide—*Phenurone*; Phenindole—*Danilone, Hedulin*; Phenylbutazone—*Butazolidin*; Perphenazine—*Trilafon*; Prednisolone 21-phosphate—*Hydeltrasol Injection*; Primidone—*Mysoline*; Prochlorperazine—*Compazine*; Promazine hydrochloride—*Sparine*; Pyridostigmin bromide—*Mesantoin*; Rauwolfia serpentina—*Raudixin, Raulin, Rautensin, Rautotal*; Reserpine—*Raurine D-Lay, Rau-Sed, Rausingle, Sandril, Serfin, Serpasil*; Sodium oxacillin—*Prostaphlin*; Tetracycline hydrochloride—*Polycycline, Steclin*; Trifluoperazine—*Stelazine*; Trimethadione U.S.P.—*Tridione*; Tolbutamide—*Orinase*.

Influenza Vaccines

Protection against impending epidemics is provided by a worldwide system of "watch" laboratories. Here viruses are isolated and forwarded to central laboratories for antigenic classification. Industrial laboratories are notified that the isolates are antigenically similar to those in the current vaccine or that there are antigenic differences which would diminish the protective value of the vaccine. In the latter case, prototype isolates are supplied so that the production of a new vaccine may be started to obtain data on safety, tolerance, and its ability to induce the formation of neutralizing antibodies. This phase is immediately followed by large-scale production of vaccine for distribution.

Protection rates averaging 75 percent have been observed for influenza A, A₁, and Asian, while average protection rates for B and B₁ are reported at 90 percent. The degree of protection depends more on the antigenic mass injected than on the route of administration. Therefore, an intradermal dose of 0.1 cc. is less effective than a subcutaneous 1 cc. dose of currently available commercial vaccines.

Reactions to influenza virus vaccines vary with the age of the subject. A very young subject is more likely to experience systemic reactions characterized by temperature rise and malaise than local reactions of erythema and induration. Conversely, in adults local reactions occur more frequently than systemic ones, and incapacitating effects are rare at the recommended dosage. However, if increased amounts of antigen are given, a corresponding rise in reaction rates will occur. Persons with hypersensitivity to egg protein may react severely to influenza vaccine, and this constitutes the sole contraindication to administration of the vaccine. According to Davenport, "A practical test is that if the subject can

eat eggs, he can be vaccinated with safety."—Reprinted from an article by GLENN O. LEASE, M.D., in the *New York State Journal of Medicine*, October 15, 1963.

Information on Use of Steroid Drugs Vital

Instant, positive medical identification for every person taking steroid drugs is essential in case of accident or emergency, according to Morton Fuchs, M.D., Clinical Assistant Professor, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, who spoke at a Hahnemann Seminar on Anabolism and Catabolism in Health and Disease.

It is estimated that some 270,000 patients with arthritis and rheumatism probably are beneficially taking steroids. But, the information must be instantly available to any physician in the emergency situation whether the patient is conscious or not, Dr. Fuchs stressed. Without this knowledge there are certain inherent hazards. However, with the knowledge the patient is on steroid therapy, any physician can adequately handle the situation without problems.

"Just as physicians are encouraging diabetic patients to wear positive identification, so should they require patients on steroids to be tagged," noted Dr. Fuchs. "It is also vital that patients seeing physicians other than the one prescribing the steroids, tell him that they are on this type of therapy," he said.

Dr. Fuchs suggested that pharmaceutical manufacturers, who were so instrumental in the research which made these drugs possible, might take a dominant role in the campaign for instant identification. In Dr. Fuchs' opinion they could make metal or plastic tags on metal chains available to physicians and pharmacists for distribution to patients.