PHARMACOPŒIAS AND FORMULARIES

THE PHARMACOPŒIA OF THE UNITED STATES

Fourteenth Revision

IT is little more than three years since the U.S.P.XIII came into force, and the Fourteenth Revision, now published, becomes official from November 1, 1950. This short interval is a measure of the rapid changes in medical, chemical and pharmaceutical requirements, and must indicate a heavy and intense programme of work accomplished by those responsible for revision. The new issue shows, by its deletions and additions, those drugs and preparations now held in repute in the United States as well as the treatment of problems of drug standardisation.

The deletions include a number of substances and preparations still in extensive use in this country. Some are well known as domestic remedies, such as Seidlitz powder, mustard plaster, cod-liver oil emulsion, saponated cresol solution, alum and sublimed sulphur. Other articles commonly prescribed, although viewed critically by some medical authorities, include caffeine citrate, prepared chalk, methylene blue, potassium citrate, tannic acid, formaldehyde solution, thymol, activated charcoal, β-naphthol and strychnine sulphate (no other salt of strychnine is mentioned). The deletion of arsenic trioxide, neoarsphenamine and sulpharsphenamine is, no doubt, due to the general adoption of antibiotics and oxophenarsine hydrochloride. The therapeutic decline of mercurials is reflected in the deletion of mercury, mild mercury chloride (calomel), mercury oleate and the mercurial ointments. A decrease in the number of vegetable drugs is in accordance with present pharmacopœial trends. Myrrh, nutmeg, red saunders wood, clove, spearmint, juniper tar and pine tar are, not surprisingly, deleted, but the omission of rhubarb, senna, stramonium, hyocyamus and ginger and their galenical preparations is less expected. Seven serological preparations are deleted, namely cholera vaccine, plague vaccine, scarlet fever streptococcus antitoxin and toxin, and bivalent, trivalent and pentavalent gas gangrene antitoxins.

Of the 203 new monographs, most are concerned with synthetic drugs, substances used in diagnosis, antibiotics and preparations, particularly tablets, capsules and injections. The synthetic compounds include the antihistamine drugs diphenhydramine hydrochloride (benadryl) and tripelennamine hydrochloride (pyribenzamine), the anti-malarial drugs chlorguanide hydrochloride (known in this country as proguanil hydrochloride), chloroquine phosphate (aralen diphosphate) and pentaquine phosphate, and the mercurial diuretics meralluride (mercuhydrin) and mercurophylline (mercuzanthin). The only new sulphonamide is phthalylsulphathiazole, with a monograph on tablets of this substance, and there are new injections for three other sulphonamides. Other monographs appearing in the U.S.P. for the first time are amphetamine, amphetamine sulphate, dicoumarol (under the title bishydroxycoumarin), dimercaprol, meperidine hydrochloride (pethidine hydrochloride), methamphetamine hydrochloride (methylamphetamine hydrochloride), naphazoline hydrochloride (privine) and tubocurarine chloride. Substances used in diagnosis include iodoalphionic acid (priodax) employed in cholecytography, methiodal sodium (skiodan), employed in pyelography, and congo red, which is used for the detection of amyloidosis and for the estimation of blood volume.

Those concerned with the preparation, standardisation and use of antibiotics will be interested in the monographs, totalling 22, on these substances,

but may be disappointed by the treatment. In the monograph on penicillin G potassium (benzylpenicillin potassium), there are details of the method of assay and tests including stability, safety and clarity of solution. On the other hand, more than half of these monographs contain little beyond a brief definition and the statement: "It complies with the requirements of the Federal Food and Drug Administration." This restricted treatment is applied to the monographs on the sodium and potassium salts of penicillin, penicillin G procaine and preparations such as ointment, tablets, troches, inhalation and aqueous and oily injections. Tyrothricin is dealt with in detail, but for aureomycin, dihydrostreptomycin and streptomycin the information is limited to Description, Solubility and Identification, and a reference to the Food and Drug Administration. In a similar way, the monographs on some biological products, including diphtheria and tetanus antitoxins and toxoids, smallpox vaccine, blood-grouping sera and Rh-typing sera, refer important requirements to the National Institutes of Health of the United States Public Health Service.

The tradition of the United States Pharmacopœia of providing a range of flavouring agents is maintained. Some of the older preparations, such as anise water, fennel water and orange flower syrup are deleted, but there are new monographs on cacao syrup, cherry juice and syrup, raspberry juice and syrup and vanilla tincture which might well be examined by pharmacists in this country. Among the pharmaceutical preparations it is interesting to note that calamine lotion is no longer prepared with bentonite magma as the suspending agent, but now contains the carbowaxes, polyethylene glycol 400 and polyethylene glycol 400 monstearate, and no glycerin. In addition to a simple benzyl benzoate lotion, a formula is given for benzyl benzoate chlorophenothane lotion containing 11·5 per cent. v/v of benzyl benzoate, 1 per cent. w/v of chlorophenothane (dicophane or D.D.T.) and 2 per cent. of w/v benzocaine emulsified with polysorbate 80 ("Tween 80"). The title amphetamine inhalant is applied to "amphetamine, usually aromatized and contained in a suitable inhaler." An identification test, assay process are given, but there is no requirement for the actual amount of amphetamine present.

The 80 injections of the U.S.P.XIV include new monographs on injections of dimercaprol, globin zinc insulin, sodium iodomethamate (iodoxyl), sodium salicylate, tubocurarine chloride and vitamin B_{12}. The general style in the injection monographs is to define the preparation as a sterile solution, provide identification tests, assay process and tolerances and refer to the "other requirements" given in an appendix. This appendix describes the solvents and vehicles which may be used, permits the addition, with certain limitations, of substances to "increase stability and usefulness," and states the excess volume to be included in single-dose and multiple-dose containers for both mobile and viscous liquids. There is a detailed statement of the testing procedures to be applied to the containers, covering a powdered glass test and whole container tests using water and acid at 121°C. Four grades of container are specified and a table shows the grade to be used for each injection. The difficult problem of controlling particulate matter in injection solutions is referred to only in a statement that "Good pharmaceutical practice also requires that each Injection, in its final container, be subjected individually to visual inspection." Details are given of the sterility tests for injections, but it is surprising to find that there is no reference to methods of sterilisation, even for thermostable substances. Consequently, the pharmacist is given no guidance or directions on the method to be used, and this seems likely to place him at a disadvantage compared with the

large-scale producer. There is the further danger that, in the absence of directions, a process involving the use of heat may be applied to a thermolabile substance.

The appendices run to 350 pages descriptive of general tests, processes, apparatus and reagents, and a series of tables. There are First and Second Sheet Supplements. The volume is an important work of refence for all concerned with the study of standards for a wide range of drugs and materials used in modern medicine. T. C. DENSTON.

ABSTRACTS (*continued from page* 605)

averaged. Injections were made in the dorsal area and the total volume injected varied from 0·2 to 1 ml., with doses ranging from 5,000 to 20,000 I.U. When the crystals of œstrone were 10 μ or less in length the average duration of œstrogenic stimulation was 10 days. When at least 50 per cent. of the crystals were 50 to 150 μ in length, the average duration from an equal dose was 24 days. A few tests were also made on oily solutions of œstrone and œstradiol monobenzoate and on aqueous suspensions of œstradiol crystals. The average duration of effect produced by these preparations was similar to or slightly less than that produced by an aqueous suspension of crystals of œstrone 10 μ or less in length. G. R. K.

Procaine Penicillin Preparations. E. Griffiths, A. J. Walker and R. A. Shooter. (*Brit. med. J.*, 1950, **1**, 761.) 113 patients with acute staphylococcal infections were treated with daily doses of a preparation consisting of 300,000 units of procaine penicillin in oil with 1 per cent. aluminium stearate and 100,000 units of sodium penicillin. The results were found to be as satisfactory as those in a similar series of patients treated with 300,000 units of procaine penicillin daily or 300,000 units of sodium penicillin in saline solution twice daily. The preparation provides detectable amounts of penicillin in the blood throughout most of the 24 hours in the majority of patients. Other preparations tried were 300,000 units /ml. of procaine penicillin in oil with 2 per cent. of aluminium stearate, and 200,000 /ml. units of procaine penicillin in oil with 2 per cent. of aluminium stearate and 100,000 units /ml. of sodium penicillin. With these latter two, the clinical results compared unfavourably with those obtained with 300,000 units of procaine penicillin. S. L. W.

***d*-Tubocurarine, Liberation of Heparin and Histamine by.** G. Reid. (*Nature*, 1950, **165**, 320.) When tubocurarine (0·25 to 15 mg.) is injected into the portal vein of the dog under chloralose there is a sharp rise of portal pressure, with a fall in systemic arterial and venous pressures. Systemic intravenous injection causes a fall of arterial and venous pressures, and the portal pressure also falls. This indicates that the rise of portal pressure is mainly due to an action of the drug within the liver itself. That this action is one of histamine liberation is shown by the antagonism of benadryl to small doses of tubocurarine given intra-portally and by the detectable loss of liver histamine with larger doses. A dose of 0·25 mg. caused a rise of portal pressure greater than that caused by the intra-portal injection of 50 μg. of histamine acid phosphate, and with large doses the effect was probably equivalent to that of several mg. of histamine. The loss of histamine, estimated by comparing the content of two pieces of liver removed before and after injection, varied from no detectable loss to a loss of 44 per cent. It was similarly shown that heparin is also liberated by *d*-tubocurarine, since, following the intra-portal injection of 4 to 15 mg., arterial blood withdrawn within 20 minutes after injection had not coagulated 24 hours later in three experiments, and in a fourth experiment the clotting-time had increased from 5 to 60 minutes. S. L. W.