PHARMACOPŒIAS AND FORMULARIES

THE ADDENDUM 1951 TO THE BRITISH PHARMACOPŒIA 1948

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The Addendum 1951 to the British Pharmacopœia 1948 presents in 114 pages several minor corrections in the first issue of the 1948 Pharmacopœia and substantial changes in 57 monographs of the latter, and adds 52 new monographs of which 41 represent new drugs. While the importance of the changes in the official specifications for existing monographs are not to be minimised, the greatest interest is in the new additions, most of which are highly significant in revealing trends in modern therapeutics. Thus the antibiotics are represented to a far greater extent than any other class of agents, more than one-fifth of the new additions falling into this class. The biologicals rank next with five members, all of which are vaccines. Three new diagnostic aids are added, of which one is indigo carmine which represents a readmission inasmuch as it appeared in the British Pharmacopœia 1932. It is used as a test for kidney function as is phenolsulphonphthalein. The third diagnostic aid is pheniodol, an iodinated diphenylpropionic acid derivative which is used for X-ray visualisation of the gall bladder. The sulphonamides are represented by only one new addition, sulphadimidine, which contrasts sharply with the number of the antibiotics which are now displacing sulphonamides as the agents of choice in chemotherapy. The antihistaminics are represented by two compounds, mepyramine maleate, which is sold under the trade names Neo-Antergan and Anthisan, and promethazine hydrochloride which is marketed as Phenergan. Other one-of-a-class admissions include dicophane, better known as DDT; dimercaprol, more familiar as BAL (British Anti-Lewisite); isoprenaline sulphate, the new and effective broncho-dilator and antiasthmatic; proguanil hydrochloride, better known as Paludrine, the anti-malarial developed in England during the war; propylthiouracil, the anti-thyroid agent; quinalbarbitone sodium which is probably better known as pentobarbital sodium, the short-acting barbiturate; *d*-tubocurarine chloride, the pure crystalline, curarising agent which is proving so effective in surgery; and vanillin which was described as a reagent in the British Pharmacopœia 1948, but now becomes an official drug.

Most interesting of the new additions is a group of eight monographs on preparations of human blood, these ranging from whole human blood, through the elements obtained ordinarily by centrifuging, that is, the concentrated red blood corpuscles and the plasma or serum, to human fibrin foam, fibrinogen and thrombin. The establishment of these standards represents a bold and realistic approach to meeting an acute need for these products, some of which are so short-lived as to complicate seriously their testing and use. It is noteworthy that neither liquid or frozen human plasma have been included, although these are popular forms of blood products elsewhere.

From this reviewer's standpoint it is especially interesting to ascertain which of the new items have official status in the United States. A check reveals that all but eighteen, of which six are preparations of human blood, now are in either U.S.P. XIV or N.F. IX, both of which have appeared since the British Pharmacopœia 1948 was published. This figure must be qualified in

that although U.S.P. XIV lists DDT (as chlorophenothane) the standards are not in effect, inasmuch as they apply to a purer grade of DDT than is now generally available.

Among the new drugs not official elsewhere in English-language compendia is ethinylœstradiol, in which the addition of the ethinyl group confers greatly enhanced oral œstrogenic effectiveness over œstradiol. Also in this category is cetrimide, a highly effective quaternary ammonium antiseptic, and isoprenaline sulphate, mentioned above. The choice of the two antihistaminics from the vast array now at hand is also of interest, since neither happens to be one of the two which are official in U.S.P. XIV.

The suggested details of the spectrophotometric method of Vitamin A have been modified to incorporate the now-familiar Morton-Stubbs correction for irrelevant absorption in the ultra-violet. The biological assay of d-tubocurarine chloride is carried out on the phrenic nerve preparation of the rat, which is in contrast to the head-drop assay on rabbits used in the United States. Directions are given for typing blood, including determination of the Rh factor in human blood.

The style of the Addendum conforms, of course, to that of the British Pharmacopœia 1948, and the volume gives the impression throughout that the usual high degree of meticulous care went into its preparation. Inasmuch as the Addendum was drafted during a period marked by the retirement of Dr. C. H. Hampshire and the assumption of the Secretaryship of the British Pharmacopœia Commission by his successor, Mr. T. C. Denston, great credit is due to both of them for the excellence of this Addendum, both in its scope and content.

CODEX MEDICAMENTARIUS GALLICUS. 7th Ed., 1949. Published by l'Ordre National des Pharmaciens by order of La Commission Permanente du Codex, pp. 1227 (including indexes).

The new French Codex constitutes the seventh edition of the French Pharmacopœia, and became official on November 1, 1950. By a decree of 1943, a Permanent Codex Commission was created, consisting of 52 regular members, of whom 36, together with 15 corresponding members, were responsible for the preparation of the monographs in this edition. The publication of the book was the responsibility of the recently-created organisation, l'Ordre National des Pharmaciens.

The outstanding differences immediately noticed between the new edition and the previous issue of 1937, are the absence of coloured plates of vegetable drugs and of the old Volume I which gave information on pharmaceutical legislation and related matters. It is proposed to publish the latter in the form of a supplement when conditions permit. The 21 monographs on newer drugs recognised during the period of the 1937 Codex have been retained. These include deoxycortone acetate, testosterone propionate, glycocoll and six sulphonamides, added by the Supplement of 1947, and amphetamine sulphate, benzyl benzoate, cetyl alcohol, cinchophen, dicophane and phenytoin, made official by decree in March, 1949. Further to these introductions, 41 monographs have been added and 290 articles deleted. Scrutiny of the lists of additions and deletions in any new edition of a national pharmacopœia provides an interesting study of medical and pharmaceutical practice in that country. The basis of selection may vary from country to country, and in the French Codex there appears a balance of those drugs for which there is a sound basis of pharmacological and con-

trolled clinical evidence and those which have, no doubt, a long reputation and sustained use in general medical practice. We thus find monographs on menaphthone and marjoram, sodium penicillin and sodium glycerophosphate. New monographs deal with synthetic drugs, including hexœstrol, stilbœstrol, nicotinamide, hexobarbitone and thiopentone sodium, surgical sutures and ligatures, surgical dressings and radio-active isotopes.

Crude drugs remain a prominent feature of the French Codex, although about 40 monographs (and the corresponding galenical preparations) have been deleted, including those on asafetida, Irish moss, copaiba, dandelion, stavesacre, guaiacum resin, musk and galls. Among those retained are a number which, in this country, fall rather within the province of the herbalist, such as centaury, sundew, fumitary, marshmallow, couch grass, hound's tongue, calamint and purple loosestrife. Microscopical description of vegetable drugs is, in general, confined to the diagnostic characters of the powder, and measurements are omitted except in a few cases where they are significant, such as the starch grains of cinnamon. The standards for aromatic drugs and spices such as cinnamon, clove and coriander do not include requirements for content of essential oil. A monograph is retained to describe the preparation of stabilised vegetable powders of drugs such as digitalis, gentian, squill and valerian. Pyrethrum flower is assayed biologically, using goldfish, and there is no chemical estimation of pyrethrins such as is generally accepted in this country and in the United States of America as a reliable method of assaying this insecticide.

The monographs on the preparation of injections and the standards for ampoules have clearly undergone careful scrutiny. A general monograph covers aqueous and oily solutions, suspensions in oil, and gland preparations (insulin, pituitary, etc.) for injection. Sterilisation is directed to be performed by heating on a boiling water-bath, steaming for 30 minutes, heating in an autoclave for 20 minutes at 110° or by tyndallisation, defined as heating for 1 hour at 70°C. on three consecutive days. This last method may be criticised as unsound in theory and inconvenient in practice. Aseptic procedure is prescribed for thermolabile substances but the method of heating with a bactericide is not recognised. Aqueous solutions for injection are required to be prepared from water with a *p*H of 6 to 8 and to be isotonic. A method of testing for pyrogens is described in detail, and is to be applied to the distilled water used or the aqueous solution comprising the injection. A separate monograph lays down standards for ampoules, which for solutions must be of uncoloured glass, but for other purposes must be of coloured glass. Ampoules and glassware used in the preparation of injections are required to comply with limit tests for total solids, alkali, arsenic and lead yielded to water under prescribed conditions.

The monographs on ligatures cover sterilised catgut, silk, silkworm gut, linen thread and synthetic ligature (nylon) as thread and plaited thread. Standards are imposed for tensile strength and for catgut there is a preliminary test for sterility, but no statement of tolerances of diameter is given. Without strict control of diameter, the standards for tensile strength may be vitiated.

Benzylpenicillin and streptomycin are the subject of long monographs with details of biological methods of assay and, for the former, of the iodimetric method. Information on the antibiotic injections and on procaine benzylpenicillin is not provided. Veterinary medicaments have been placed with other preparations from which they differ only in their application. Phenothiazine, which is widely used in this country in veterinary practice and

rarely, if ever, in human medicine, is not indicated as being a veterinary preparation but is provided with a range of adult human doses.

Doses are no longer stated at the foot of each monograph, but are given in posological tables at the end of the book, showing maximum and usual doses for adults and children.

It is clear that the monographs carried forward from the previous edition have been carefully studied and revised in many particulars in order to provide useful information and reasonable standards of purity.

Congratulations are due to those responsible for the detailed work of preparation and to l'Ordre National des Pharmaciens for discharging its duties as publisher in so successful a manner.

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ABSTRACTS (*Continued from page 602*)

injection. Compounds for assay should be given either at the time of, or 24 hours before, the inoculation of the eyes. S. L. W.

Vitamin D, Criterion for Dosage of. P. Fournier. (*C.R.Acad. Sci., Paris*, 1951, **252**, 1019.) In rats on a suitable diet, the fæcal excretion of calcium is increased 3 times when they are deprived of vitamin D, although the elimination in the urine is unaffected. Actually, in place of the determination of total calcium, it is more convenient to determine the ratio of calcium to an inert substance (titanium dioxide) added to the diet. The curve of variation of calcium excreted with doses of vitamin administered is logarithmic. Response to treatment may be seen earlier than with the other criteria generally employed, and it is not necessary to sacrifice the animals. A statistical study, using a large number of animals, is desirable to determine the relative accuracy of this process. G. M.

BACTERIOLOGY AND CLINICAL TESTS

***Pseudomonas pyocyanea* Contamination of Disinfectant Solutions.** E. J. L. Lowbury. (*Brit. J. industr. Med.*, 1951, **8**, 22.) The occurrence of *Pseudomonas pyocyanea* infections in wounds adequately covered using a "no-touch" dressing technique led to the testing for sterility of a number of solutions, including 2 per cent. soap, 1 per cent. cetrimide and 10 per cent. Dettol, actually in use in hospital dressing stations and operating theatres. All of 18 samples of soap solution, 6/23 of cetrimide solution and 3/9 of Dettol solution were contaminated by *Ps. pyocyanea*. The infected samples were all taken from corked bottles and a higher proportion of positive tests was obtained from the cork than from the solutions. After replacing all the corked bottles by screw-capped bottles, no contamination of the contents by *Ps. pyocyanea* was found. Of 541 swabs examined in the year preceding the change of container, 18·5 per cent. contained *Ps. pyocyanea*. Of 104 examined in the succeeding three months, only 3 (2·8 per cent.) contained the organism, 2 being from old cases. The survival of the organisms in concentrations which would be lethal to them in ordinary *in vitro* tests is considered to be due to the presence of growth-promoting substances in the cork, possibly aided by a protective envelope of dried exudate from the wound in which the contaminating organism had previously grown. It is recommended that liquids for application to wounds be dispensed in small screw-capped bottles and sterilised after filling, either by autoclaving or, if this is impossible, by boiling. H. T. B.