ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Aspirin, Phenacetin and Caffeine, Determination of. E. G. Wollish, R. J. Colarusso, C. W. Pifer and M. Schmall. (*Analyt. Chem.*, 1954, **26**, 1753.) A method is given whereby aspirin and phenacetin are determined by non-aqueous titration, the caffeine being estimated iodometrically or colorimetrically. Aspirin, phenacetin and caffeine are first extracted from the tablet mass in an acidic medium with a solvent mixture. For the aspirin determination, the solvent is evaporated and the residue is taken up in dimethylformamide, the aspirin being titrated with lithium methoxide using thymol blue as indicator; usual tablet constituents do not interfere, with the exception of stearic acid, which causes a slight positive error. Phenacetin is determined by hydrolysis to phenetidine hydrochloride, extraction of the base from alkaline solution, and potentiometric titration in chloroform with perchloric acid; caffeine, which is also extracted, is too weak a base to interfere under the specified conditions. A method for caffeine is recommended which involves the precipitation of caffeine periodide with a measured excess of 0·1 N iodine followed by titration of the excess with sodium thiosulphate. A technique for the determination of antihistamines or codeine salts is described. Recovery results using tablet mixtures of different composition, including excipients, gave a standard deviation of 0·19 for aspirin and 0·8 for acetophenetidine, indicating a satisfactory precision. R. E. S.

Oxytetracycline, Separation of Chlortetracycline from. R. J. Hickey and W. F. Phillips. (*Analyt. Chem.*, 1954, **26**, 1640.) Methods are given for counter-current distribution and paper chromatographic resolution of mixtures containing chlortetracycline and oxytetracycline. The paper chromatography was qualitative but the countercurrent distribution procedure could be utilised for qualitative or quantitative work and also on a preparative basis. Counter-current distribution separation was studied in the glass apparatus developed by Craig. The lower, aqueous phase, was 0·1 N hydrochloric acid in equilibrium with an equal volume of *n*-butanol, the resulting butanol being the upper phase. Chlortetracycline and oxytetracycline (0·1 g. of each) were distributed in the aqueous phase of the first four tubes, the volume of each phase being approximately 11 ml. per tube; a total of 100 tubes was used for distribution at 29° C. When the distribution was completed, the content of each tube was shaken with 10 ml. of light petroleum, and the phases were separated and assayed microbiologically. For paper chromatographic separation the method of Peterson and Reineke (*J. Amer. chem. Soc.*, 1950, **72**, 3598) was adapted for use with strips of Schleicher and Schuell No. 507 filter paper using 25 per cent. glacial acetic acid, 50 per cent. *n*-butanol and 25 per cent. water as the solvent system. R. E. S.

Pharmaceutical Preparations, Chromatographic Procedure for the Assay of. D. Banes. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 580.) The method depends upon the incorporation of tablets, mixtures, elixirs, etc., into a chromatographic

column, from which the active ingredients are extracted by elution. For the rapid analysis of tablets of digitoxin, a sample equivalent to 3 mg. of digitoxin is treated with water and formamide and mixed with 7 g. of Celite to form part of a column. After washing the column with *iso*octane, digitoxin is eluted with benzene-chloroform (3 : 1). On evaporation of the solvent, the glycoside is obtained in a white crystalline form and may be determined quantitatively by the usual methods, for example, measurement at 495 mμ of the colour produced in the alkaline picrate reaction. The presence of aglycones may be detected by the Keller-Kiliani reaction. The analysis of digitoxin tablets may be completed in a little over 3 hours. Elixirs containing strychnine and quinine may be concentrated, treated with 6 N hydrochloric acid and mixed with Celite to form part of a column from which, after washing with ether, strychnine is eluted with chloroform and determined by measurement of the ultra-violet absorption at 256 mμ in a solution with hydrochloric acid. Quinine may be eluted with water and determined separately. A similar method may be employed in the analysis of mixtures of acetylsalicylic acid, phenacetin and caffeine, after removal of the acetylsalicylic acid by the A.O.A.C. method.

G. B.

Stilbœstrol in Tablets, Determination of. J. M. Goodyear, L. S. Hatfield and M. M. Marsh. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 605.) The determination depends on the production of a yellow substance of unknown composition, by the ultra-violet irradiation of stilbœstrol. A sample of powdered tablets, equivalent to about 1 mg. of stilbœstrol is warmed with 10 ml. of water for 15 minutes, cooled and made up to 50 ml. with glacial acetic acid. A quantity is placed in a quartz tube and irradiated by a suitable mercury arc lamp without filter for 7 minutes. The light absorption is determined at 420 mμ. A standard solution is irradiated at the same time to compensate for variation in lamp intensity, and the quantity of stilbœstrol is read from a standard curve. Other solvents require different exposure times for the development of maximum colour, but the above solvent seems to be the most effective for the extraction of stilbœstrol from tablet material. In the ultra-violet absorption method, a methanolic extract containing about 0·005 per cent. of stilbœstrol is prepared from the tablets. Five ml. of the solution is mixed with 0·5 ml. of 0·5 N hydrochloric acid and dehydrated methanol to 20 ml. Similarly, 5 ml. is mixed with 5 ml. of 0·5 N sodium hydroxide and dehydrated methanol to 20 ml. Standard solutions are prepared in the same way, and the absorption determined at 280 mμ, the result being calculated by equations. The precision of the method is about 1·5 per cent., compared with 1 per cent. for the irradiation method.

G. B.

Theobromine and Caffeine, Analysis of Mixtures of. J. W. Miles and D. T. Englis. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 589.) Caffeine and theobromine have similar ultra-violet absorption spectra when examined in acid solution, the maxima at 273 mμ being almost identical. On making the solutions alkaline, little change occurs in the spectrum of caffeine, but in the case of theobromine, enolisation apparently takes place, accompanied by a considerable increase in the absorption between 220 and 254 mμ. In the analysis of mixtures, the quantity of theobromine can be calculated from the difference in absorption of solutions in 0·1 N sodium hydroxide and 0·1 N hydrochloric acid at 240 mμ. The quantity of caffeine can be calculated from the absorption at 273 mμ in acid solution, after allowing for the amount of theobromine present. Alternatively, the quantity of theobromine and caffeine

may be calculated from the absorption at 240 and 273 mμ in 0·1 N sodium hydroxide. A more accurate method involves complete separation of the components, but of course takes longer. G. B.

Veratridine and Cevadine, Separation of, by Partition Chromatography. G. R. Svoboda and L. M. Parks. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 584.) Solutions of pure veratridine and cevadine in benzene and chloroform with the addition of up to 10 per cent. of ethanol were shaken with aqueous buffer solutions, *p*H 5·8 to 7·5, and the partition coefficients determined after titration of a sample of the organic layer with perchloric acid in acetic acid. The results indicated that the best separation of veratridine and cevadine could be obtained with chloroform and buffer solution, *p*H 4·25. In chromatographic experiments using columns of silicic acid with buffer solution *p*H 4·0, 4·25 and 4·5, and chloroform as eluant, recoveries of veratridine and cevadine from veratrine samples averaged 80 per cent., the identity and purity of the fractionated alkaloids being checked by ultra-violet absorption and titration. Veratridine and cevadine were also separated chromatographically from the alkaloidal mixture obtained by extraction of sabadilla seed with Skellysolve B. G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Glucose, Fructose, Galactose and Sorbitol, Blood Sugar Levels and Urinary Excretion of Intravenously-Infused. V. P. Seeberg, B. Whitney and D. Goldman. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 592.) Groups of rabbits received the above substances, administered intravenously in the form of 10 per cent. solutions, a total dose of 1·5 g./kg. being given at 1 g./kg./hour, representing a usual clinical infusion rate. The total urinary excretion averaged 4·2 per cent. for glucose, 9·8 per cent. for fructose, 29·6 per cent. for galactose and 17·7 per cent. for sorbitol. Somewhat lower blood sugar levels were obtained with fructose than with glucose, but the difference was not significant and might have been due to the greater urinary excretion of fructose. Galactose produced the highest and most persistent blood levels which, together with a high urinary excretion, confirm that the substance has a low utilisation rate. The administration of sorbitol gave rise to relatively low blood sorbitol levels, accompanied by an increase in the concentration of reducing sugars. The identity of these sugars, derived from sorbitol, was not established. During the fourth hour of the tests, very little sorbitol was excreted, although a fairly high blood level remained. The explanation suggested is that sorbitol undergoes conversion into a substance giving a positive sorbitol test but differing from sorbitol in being reabsorbed by the kidney tubules. G. B.

BIOCHEMICAL ANALYSIS

Glycerides in Blood, Estimation of. R. D. Stewart. (*Canad. J. Biochem. Physiol.*, 1954, **32**, 679.) A method is described for the estimation of neutral glycerides in whole blood. 0·1 ml. of blood is added to 20 ml. of a mixture of 3 parts of pure absolute ethanol and 1 part of absolute ether, thoroughly mixed and filtered quantitatively through Whatman No. 1 filter paper, the paper being washed with a further 5 ml. of the solvent. The filtered extract is evaporated

to dryness on a steam bath in an atmosphere of nitrogen, 10 ml. of chloroform added and the soluble lipid transferred to a small, round bottomed distilling flask and the solvent evaporated under nitrogen. Two ml. of a saturated aqueous solution of potassium hydroxide is then added together with 0·1 ml. of ethanol and saponification allowed to proceed for 5 minutes at 80 to 100° C. The solution is then acidified by cautious addition of 1 ml. of water and 1 ml. of 15 M sulphuric acid. Two ml. of periodic acid solution (0·01 M sodium periodate in 0·15 M sulphuric acid) is then added and oxidation of the glycerol present allowed to proceed for 45 minutes at room temperature. One ml. of 5 per cent. stannous chloride solution is then added to stop the reaction, then 3 ml. of 5 M sulphuric acid and the formaldehyde from the oxidised glycerol distilled into 1 ml. of sodium sulphite solution (4 per cent. sodium sulphite in 1 per cent. ethanol) and 5 ml. of distillate collected. Three ml. of the resulting solution is transferred to a boiling tube together with 5 ml. of chromotropic acid reagent (4 ml. of a 5 per cent. aqueous solution diluted to 100 ml. with 15 M sulphuric acid). The tube is placed in a boiling water bath for 30 minutes, cooled and 2 ml. of 9 M sulphuric acid added. The resulting violet colour is read in a spectrophotometer at 540 mμ. Reagent blanks of the ethanol-ether mixture are run alongside. Corrections have to be applied for phospholipids present which interfere with the determination. Results are given for neutral fat in normal and diabetic patients. G. F. S.

Serum Vitamin B_{12}, Estimation of. R. H. Girdwood. (*Brit. med. J.*, 1954, **2**, 954.) A method is described for the estimation of vitamin B_{12} in serum, using *Lactobacillus leichmannii* which gives results in 24 hours. It is valuable in the investigation of the pathogenesis of complex cases of megaloblastic anæmia. 20 ml. of venous blood is put into a sterile container, allowed to clot, and the serum removed by centrifuging. The serum is prepared by the method of Rosenthal and Sarett. To 5 ml. of serum add 5 ml. of 1 per cent. acetate-buffer at *p*H 4·6 and 20 ml. of distilled water. Mix, place the tube in a boiling water bath for 30 minutes, cool and centrifuge. Adjust 9 ml. of this solution carefully to *p*H 6·9 $\pm$ 0·1 with dilute sodium hydroxide and make up to a total volume of 15 ml. (= a final dilution of 1 : 10 of the original serum.) The material is now assayed for total vitamin B_{12} using the medium of Thompson, Dietrich and Elvehjem, modified by the addition of thioglycollic acid and the omission of ascorbic and fumaric acids. The cyanocobalamin standard and the diluted serum are added prior to autoclaving or using aseptic precautions. The growth of the test organism is estimated by measuring the turbidity after incubation for 16 hours at 37° C. In 34 out of 36 patients with pernicious anæmia in relapse, the serum level was less than 130 $\mu\mu$g./ml. and in 11 of these less than 50 $\mu\mu$g./ml. All responded to treatment with vitamin B_{12}. In 50 control cases the mean serum vitamin B_{12} level was 320 $\mu\mu$g./ml. (range 50–870 $\mu\mu$g./ml.) and in only 3 cases less than 130 $\mu\mu$g./ml., two of these showing clinical features suggesting pernicious anæmia. G. F. S.

CHEMOTHERAPY

Dehydroacetic Acid and *p*-Chloro-*m*-xylenol, Antimicrobial Activity of a Combination of. R. L. Stedman, S. L. Engel and I. M. Bilse. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 622.) Tests for bacteriostatic and fungistatic action against *Micrococcus pyogenes* var. *aureus*, *Candida albicans* and *Trichophyton mentagrophytes* were carried out by a serial dilution technique.

Bactericidal and fungicidal properties were assessed by a modified phenol coefficient test. Solutions in water containing 30 per cent. of polyethylene glycol 300 were employed. In preparations containing both dehydroacetic acid and chloroxylenol, the bactericidal and fungicidal effects due to the components were generally additive, whereas in the inhibitory tests there was an enhancement of effect, resulting in lower concentrations being required to prevent growth. *In vitro* tests were also performed with a preparation containing 10 per cent. of dehydroacetic acid and 2 per cent. of chloroxylenol dissolved in water containing 30 per cent. of polyethylene glycol 300, with the addition of 15 per cent. of *iso*propanol. This preparation was more effective against organisms commonly associated with superficial mycoses than commercial preparations of fatty acids, unsaturated carboxylic acids, salicylic and benzoic acids, or malachite green. An ointment containing 20 per cent. of dehydroacetic acid and 5 per cent. of chloroxylenol in a base consisting of equal quantities of polyethylene glycol 300 and carbowax 1400, tested *in vitro* against organisms associated with vaginal mycosis and trichomoniasis was found to be superior to commercial products containing silver picrate, 5:7-diiodo-8-hydroxyquinoline, boric acid, sulphathiazole, lactic acid and acetic acid.

G. B.

Magnamycin B, Antibiotic from *Streptomyces halstedii*. F. A. Hochstein and K. Murai. (*J. Amer. chem. Soc.*, 1954, **76**, 5080.) Magnamycin B, a new antibiotic, was isolated from fermentation beers of *Streptomyces halstedii*. It was obtained as a crystalline compound from the mother liquors resulting from the crystallisation of crude magnamycin. It melts with decomposition at 141 to 144° C. and has $[\alpha]_D^{25}$ −35°. The ultra-violet absorption spectrum shows a strong absorption peak at 278 mμ and the infra-red absorption spectrum is characteristic. Analyses of magnamycin B and some of its derivatives suggest a molecular formula of $C_{41-2}H_{67-9}NO_{15}$. It resembles magnamycin in its antibacterial spectrum, its low toxicity, and in its fundamental chemical nature. The spectral studies indicate that it contains an $\alpha:\beta:\gamma:\delta$-unsaturated ketone, in contrast to the $\alpha:\beta$-unsaturated ketone system of magnamycin. The monoacetyl, tetrahydro, and monoacetyltetrahydro derivatives had the same biological activity as magnamycin B itself. A. H. B.

PHARMACY

NOTES AND FORMULÆ

Adrenaline Solutions, Deterioration of. D. E. R. Argent and O. P. Dinnick. (*Lancet*, 1954, **267**, 947.) As a result of several cases where large overdoses of adrenaline were administered without ill effect, presumably owing to deterioration of the solutions, the authors investigated stock solutions by assay on the blood pressure of the cat under chloralose anæsthesia and on the vasoconstrictor effect produced in the perfused hind limb of the rat. Of 4 samples of 1:1000 adrenaline solution taken from stock, 2 were completely inactive on both preparations. By comparison, using a freshly prepared solution made according to the B.P., 0·1 μg. produced a distinct rise in blood pressure and vasoconstriction in the limb. After freshly preparing solutions of different dilutions, transferring them to gallipots and glass containers, and exposing them to the air at room temperature for 30 minutes, a 1:1000 and a 1:10,000 solution remained fully potent, but a 1:100,000 or more dilute solution was completely inactive. After 2 hours exposure to air at room temperature the 1:10,000

solution showed 50 per cent. loss of activity, but the 1 : 1000 solution remained potent for about 12 hours. A 1 : 1000 solution drawn into a syringe (glass and metal, with ceramic piston) showed no loss of activity after 6 hours. From the experiments it is concluded that (*a*) stock solutions of adrenaline are not always potent, (*b*) dilution of the stock solution produces a fall in potency, (*c*) exposure of the solution to air in glass or metal containers produces a marked loss in activity, (*d*) solutions drawn up into syringes with brief exposure to air do not appear to suffer loss of potency. As manufacturers recommend that adrenaline should not be used after storage for 18 months the authors suggest that containers of adrenaline should be date-stamped at the time of manufacture in order to avoid using stock which may have deteriorated. J. R. F.

Barbiturates, Determination of Stability of, in Solution. H. Nuppenau. (*Dansk Tidsskr. Farm.*, 1954, **28**, 194.) Methods for the determination of decomposition products of barbituric acid derivatives are not of general application, since the decomposition reaction is not always the same. A direct determination of unhydrolysed compound is possible by using the cobaltamine reaction. It is important that the reagents used should be anhydrous. In the author's method the blank contains cobalt reagent and chloroform only, as with the addition of *iso*propylamine its colour varies with time. The chloroform used is dried over sodium sulphate, and the cobalt acetate by heating at 105° C. for 2 hours. The barbituric acids were recrystallised twice from 50 per cent. ethanol, then dried at 105° C. to constant weight. Methanol was dried by distillation over magnesium turnings, using iodine as catalyst. Standard curves were determined by treating 2 to 5 mg. of the barbituric acid, dissolved in chloroform, with 5·00 ml. of 0·125 per cent. cobalt acetate in methanol, 5·00 ml. of 25 per cent. v/v solution of *iso*propylamine in methanol (Note: cool before making up to volume), and chloroform to 25 ml. The extinction was determined at 565 mμ. Owing to the absence of *iso*propylamine in the blank, the curves do not go through the origin, and the amount of barbituric acid is given by an equation where y is the extinction and x the amount of barbituric acid:—

Barbituric acid derivative	Equation
Barbitone	$y = 0{\cdot}049x + 0{\cdot}023$
Ethylallylbarbituric acid	$y = 0{\cdot}045x + 0{\cdot}024$
Allobarbitone	$y = 0{\cdot}042x + 0{\cdot}025$
Allyl*iso*propylbarbituric acid	$y = 0{\cdot}040x + 0{\cdot}023$
Amylobarbitone	$y = 0{\cdot}037x + 0{\cdot}025$
Hexobarbitone	$y = 0{\cdot}030x + 0{\cdot}025$
Methylphenobarbitone	$y = 0{\cdot}030x + 0{\cdot}024$
Phenobarbitone	$y = 0{\cdot}047x + 0{\cdot}023$
Cyclobarbitone	$y = 0{\cdot}041x + 0{\cdot}025$

The presence of hydrolysis products does not interfere with this determination. G. M.

Cascara sagrada, Effect of Age and Heat on the Ferment in. M. C. Gosselin and C. W. Bauer. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 569.) To test the hydrolytic activity of samples of cascara, aqueous extracts were prepared and included in a digestion mixture, containing normal saline, phosphate buffer (*p*H 7), solution of potato starch (1 per cent.) and water. The digestion mixtures and controls containing water in place of the cascara extract, were maintained at 40° C. and tested at minute intervals until the starch was digested, as shown by the disappearance of the blue colour on the addition of a drop of iodine solution used as external indicator. A serial dilution and titration method

were also employed to obtain more detailed information. The hydrolytic substance appeared to be stable to storage over long periods, and to heat at 100° C. Although the substance was partly inactivated by dry heat at 100° C., the activity was restored if the maceration mixture was brought to the boil in preparing the extract. The cascara sample collected in 1951 showed more activity than the 1949 and 1950 samples. By a process of fractional precipitation the hydrolytic principle was extracted from powdered cascara as a black, shiny, glass-like sticky substance, soluble in water, melting point about 220° C., yield about 10 per cent. G. B.

***Digitalis purpurea* and *Digitalis lutea*, Preliminary Studies Concerning the Lyophilised Water-soluble Extracts.** F. P. Cosgrove and E. P. Guth. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 266.) Extracts were prepared by freeze-drying infusions of oven-dried or freeze-dried leaves. The extracts were light-brown in colour, slightly hygroscopic, and readily soluble in water, forming clear solutions in concentrations as high as 20 per cent. Comparable results were obtained when equivalent concentrations of extracts and tinctures, prepared from corresponding samples, were assayed by the frog heart and colorimetric methods. The extracts were stable for at least 60 days. There was no significant difference between extracts from oven- and freeze-dried material when tested by the frog method, but considerable variation was obtained in the colorimetric method, possibly owing to differences in the proportion of primary and secondary glycosides. G. B.

PHARMACOLOGY AND THERAPEUTICS

***p*-Aminosalicylic Acid, Mechanism of Goitrogenic Action of.** D. A. W. Edwards, E. N. Rowlands and W. R. Trotter. (*Lancet*, 1954, **267**, 1051.) This paper reports the results of experiments to test the hypothesis that *p*-aminosalicylic acid acts by blocking the organic binding of iodide in the thyroid. The effect of a single dose of 5 g. of sodium *p*-aminosalicylate on the concentration of iodide in saliva was measured in 4 patients who had previously received large therapeutic doses of radio-iodine, and no change was found. Further experiments showed that the compound, unlike thiocyanate and perchlorate, does not cause the discharge of accumulated iodide from the thyroid and therefore does not exert its antithyroid effect by interfering with the iodide-concentrating mechanism. Two thyrotoxic patients were given 5 g. of sodium *p*-aminosalicylate by mouth, and 1 hour later an oral tracer-dose of radio-iodide; the amount of radio-iodine in the thyroid was measured. The thyroid count rose rapidly and levelled off after an hour suggesting that the compound was exerting a thiouracil-like action. An oral dose of 200 mg. of potassium perchlorate was given to discharge any iodide that had not been organically bound in the synthesis of thyroid hormone. The proportion of radio-iodine discharged from the thyroid, expressed as a percentage, was used to measure the effectiveness of the compound in blocking hormone synthesis. In one patient about 30 per cent. of the accumulated radio-iodine was discharged; in the other more than 95 per cent. was discharged. Five other patients, all euthyroid and without goitres were similarly examined. The radio-iodine was given 1½ to 2 hours after the dose of 4 to 5 g. of sodium *p*-aminosalicylate and followed an hour later by 200 mg. of potassium perchlorate. The percentages of radio-iodine discharged were 25, 30, 75, 85 and 95. These results indicate that *p*-aminosalicylic acid is a moderate inhibitor of hormone synthesis in the dosage generally used. Presumably the low incidence of

goitre and myxœdema in patients receiving sodium *p*-aminosalicylate is partly explained by the fact that it is a relatively feeble inhibitor and partly because the plasma-level falls rapidly after a therapeutic dose. In those few patients who do develop goitres or myxœdema the compound must act as a more nearly complete inhibitor of hormone synthesis, possibly because of differences in the rate of excretion. S. L. W.

Chlortetracycline and Erythromycin Therapy for *Str. pyogenes* in Burns. E. J. L. Lowbury and J. S. Cason. (*Brit. med. J.*, 1954, **2**, 914.) Oral chlortetracyline and erythromycin were compared in the treatment of burns infected with *Str. pyogenes* sensitive to both antibiotics. Over a period of 8 months cases were admitted alternately to the chlortetracycline and erythromycin treatment groups; in each series there were 24 burns in 21 patients. Treatment was given for 6 days to patients over 1 year of age on the appearance of streptococci of Lancefield's group (*Str. pyogenes* on any burn). Patients under 6 years of age were given 500 mg. of chlortetracycline daily or 400 mg. of erythromycin; for those over 6 years of age the respective doses were 1 g. and 600 mg. All the burns in the trial were free of *Str. pyogenes* after 3 or more days' treatment with either antibiotic. A slightly larger proportion of burns in the erythromycin than in the chlortetracycline series did not show *Str. pyogenes* during the first 3 days of treatment. Reappearance of streptococci on burns from which the organisms had been cleared was infrequent. All of 7 burns (on 5 patients) from which chlortetracycline-resistant streptococci had been isolated were free from streptococci after a course of treatment with erythromycin. Provided therapy begins at least 3 days before the operation the use of either antibiotic improves the results of skin-grafting operations by eliminating interference with the healing process by *Str. pyogenes*. The use of erythromycin is advocated in the treatment of streptococcal infection of burns in severely ill patients in whom the toxic side-effects commonly found during chlortetracycline therapy might hinder recovery; but in such patients frequent examination of the burns and nares for staphylococci resistant to erythromycin is advisable. S. L. W.

β-Diethylaminoethyl Diphenylpropylacetate, Inhibitory Effects of, *In Vitro*. J. R. Cooper, J. Axelrod and B. B. Brodie. (*J. Pharmacol.*, 1954, **112**, 55.) The inhibitory action of β-diethylaminoethyl diphenylpropylacetate upon the biotransformation systems described in (*J. Pharmacol.*, 1954, **112**, 49) was extended by *in vitro* studies on rat and rabbit liver slices and homogenates. The liver slices from animals pretreated with the inhibitor, when incubated in Krebs-Ringer with hexobarbitone, pentobarbitone and quinalbarbitone, metabolised these drugs more slowly than slices from untreated animals. Similar results were obtained for the metabolism of aminopyrine, meperidine and dibenamine by de-alkylation, for the conjugation of morphine to form a glucuronide and for the conversion of codeine to morphine by ether cleavage. Also, the parent acid, diphenylpropylacetic acid, which had inhibitory activity equal to that of the ester on other drug metabolism systems, markedly depressed the de-amination of amphetamine to the corresponding ketone (the ester inhibitor could not be investigated because of its interference with the estimation of amphetamine). The inhibitory action of the acid and ester appears to be located in the supernatant fraction of the cell homogenate, i.e., in the microsomes and/or the soluble part of the cell. The acid inhibitor had no effect on triphosphopyridine nucleotide (TPN)-cytochrome C reductase, nor on cytochrome oxidase activity, although all the metabolic pathways affected had in

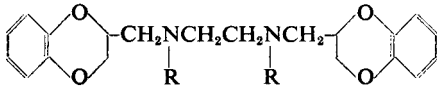
common a requirement for reduced TPN and oxygen. Although the ester and acid were equally effective at the cellular *in vitro* level, the ester was much more effective *in vivo*. Diethylaminoethanol had no inhibitory activity. G. P.

β-Diethylaminoethyl Diphenylpropylacetate, Potentiating Action of. J. Axelrod, J. Reichenthal and B. B. Brodie. (*J. Pharmacol.*, 1954, **112**, 49.) β-diethylaminoethyl diphenylpropylacetate hydrochloride (SKF 525A), which by itself has almost no pharmacological action, prolonged the action of hexobarbitone, pentobarbitone, meperidine, ephedrine and aminopyrine by inhibiting their rate of metabolic transformation in the body. This was demonstrated for hexobarbitone in rats and pentobarbitone and hexobarbitone in dogs by determining the 'biological half-life' of the barbiturates and relating this to the return of the righting reflex after anæsthesia with the barbiturate. Both duration of action and half-life were increased up to fivefold by the compound. Meperidine demethylation to normeperidine in mice, and demethylation of ephedrine to norephedrine and of aminopyrine to 4-aminoantipyrine in dogs were also inhibited by the compound. It seems probable that in its inhibitory action, the ester is acting upon a factor common to the metabolising enzyme systems. Since the drug is relatively non-toxic to animals even in large doses, the enzyme systems involved would appear not to serve a vital function. G. P.

Diphenylhydroxyacetic Acid Derivatives as Central Analgesics. J. Klosa. (*Arch. Pharm. Berl.*, 1954, **287**, 321.) Derivatives of αα-diphenyl-α-hydroxyacetic acid have been shown to have a central analgesic action. In particular, the β-dimethylaminoethyl ester (diphemin) has a high spasmolytic action with extremely low toxicity, and has been recommended for rhinitis. Etherification of the hydroxyl group causes an increase in the analgesic action, most marked in the ethoxy compound of diphemin. In animal trials the central analgesic effect exceeded that of dolantin, while it did not interfere with breathing. The toxicity is small, and there is a slight sedative action. Other alkoxy compounds are much weaker, but if etherified with β-dialkylaminoethanols, an additional strong antihistamine action is observed. These compounds approach morphine in their effect, although they have no quaternary carbon atom. As they have a distinct sedative effect, they do not produce a craving. G. M.

Ethyl Biscoumacetate and Phenylindanedione, Effect of Oral Vitamin K_1 on the Action of. J. N. M. Chalmers, M. F. Dixon and W. Polack. (*Brit. med. J.*, 1954, **2**, 956.) A series of experiments are reported on the effects of oral doses of vitamin K_1 on groups of healthy subjects taking regular doses of ethyl biscoumacetate or phenylindanedione. The dose of vitamin K_1 was 100 mg., given orally as a finely dispersed emulsion. Prothrombin activities were estimated at frequent intervals by Quick's method. In six normal subjects prothrombin activities were veering towards normal in 4 hours after administration of vitamin K_1 were normal in 24 to 30 hours, and remained normal for 2 to 3 days even though administration of ethyl biscoumacetate was continued. Similarly with phenylindanedione, recovery of prothrombin activity occurred in 24 to 48 hours, even with continued phenylindanedione therapy. In normal subjects and hospital patients, the average time for recovery of prothrombin time after ethyl biscoumacetate was $44{\cdot}3 \pm 7{\cdot}4$ hours, but after vitamin K_1 this was reduced to $10{\cdot}3 \pm 4{\cdot}8$ hours. With phenylindanedione the times were $61{\cdot}6 \pm 10{\cdot}9$ and $12{\cdot}6 \pm 6{\cdot}3$ hours respectively. Thus oral vitamin K_1 antagonised the effects of ethyl biscoumacetate and phenylindanedione, in contrast to the water soluble vitamin K_1 analogues which orally and parenterally are very ineffective. G. F. S.

Ethylenediamines as Adrenergic Blocking Agents. A. P. Swain and S. K. Naegele. (*J. Amer. chem. Soc.*, 1954, **76**, 5089.) The preparation of ethylenediamines of general formulæ I and II is described, in which R = H, CH_3 or C_2H_5 and n = 2 or 3.



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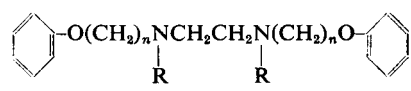

II

Some of the compounds had marked adrenolytic and sympatholytic activity by oral and parenteral routes of administration; the most active were *NN'*-bis-(1 : 4-benzo-dioxan-2-ylmethyl)- and *NN'*-bis-(2-phenoxyethyl)-ethylenediamines (I, R = H and II, R = H; n = 2 respectively). A. H. B.

Ethyleneimine Derivatives, Carcinogenic Activity of. A. L. Walpole, D. C. Roberts, F. L. Rose, J. A. Hendry and R. F. Homer. (*Brit. J. Pharmacol.*, 1954, **9**, 306.) Carcinogenic and mutagenic activity has been found with a series of monofunctional ethyleneimine derivatives, notably the *N*-acyl compound, with ethyleneimine itself and with β-propiolactone. The compounds were dissolved in a suitable vehicle, usually arachis oil, and injected subcutaneously, twice weekly, into rats and mice. A slight degree of carcinogenic activity was found with control injections of the arachis oil, in rats. Three ethyleneiminosulphonyl alkanes, similarly tested, had no carcinogenic activity, despite the fact that, in previously conducted experiments, tumour growth inhibition was found with both bis-(ethyleneiminosulphonyl)-alkanes and bis-(ethyleneiminocarbonyl)-alkanes. None of the compounds tested in the present experiments had any tumour-inhibiting activity in rats bearing the Walker carcinoma. This lack of inhibitory activity in the monofunctional ethyleneimines, together with the difference between sulphonyl- and carbonyl-compounds in carcinogenic activity, was taken to suggest a different site of action of these compounds from that of the polyfunctional ethyleneimines, i.e., the site within the cell involved in carcinogensis may be distinct from that concerned with tumour inhibition. The relationship between structure and carcinogenic and inhibitory activity is discussed. G. P.

Hexylresorcinol as an Air Disinfectant. O. M. Lidwell and R. E. O. Williams. (*Brit. med. J.*, 1954, **2**, 959.) The effect of aerosols of hexylresorcinol, prepared in "ærovap" vaporisers, on the incidence of colds during the winter 1951–52 have been tested in 3 office rooms. The results were compared with 5 similar rooms, 3 with dummy vaporisers and 2 with no vaporisers. Each room had a capacity of 26,000 cu. ft. and a staff of 40 to 45 people, equally distributed with respect of age, sex, and status. Each vaporiser was designed to yield 30 mg. of hexylresorcinol an hour. Records of illness, particularly colds, were obtained weekly by personal inquiry. Air samples were analysed bacteriologically 4 times during the winter. A record was made in each case of the general count of viable bacteria, of mouth streptococci and of *Str. salivarius*. The results showed that the aerosols of hexylresorcinol had no detectable effect on the bacterial content of the air, on the number of colds recorded or on the number of days sick absence. A short term test, using higher concentrations of hexylresorcinol, showed that a reduction of the bacterial content of the air could not be obtained without risk of respiratory tract irritation from the hexylresorcinol. G. F. S.

Histamine Liberation *In Vitro* and Mode of Binding in Tissues. A. L. Grossberg and H. Garcia-Aracha. (*Science*, 1954, **120**, 762.) This paper describes the release of histamine from dog liver homogenates. Dog liver, perfused blood free, was ground with sand in isotonic (0·32 M) sucrose. The particulate fraction was brought down to 5000 g. for 30 minutes in the cold, washed twice, and resuspended in the sucrose solution. The total histamine present in this fraction varied from 3 to 10 μg./g. weight of the original tissue and non-sedimentable histamine amounted to 5 to 10 per cent. of the total. Addition of 2 to 4 volumes of distilled water immediately and quantitatively converted all the histamine to the non-sedimentable form, even at 0° C. Histamine was totally released by treating the suspension with 90 per cent. acetone in the cold. Freezing and thawing the suspension quantitatively released the bound histamine. Addition of lytic substances—saponin, sodium taurocholate and lysolecithin—rapidly and completely liberated histamine. Addition of known histamine liberators, 1 : 10-diaminodecane, propamidine or compound 48/80, at final concentrations of 10 to 200 μg./ml. progressively released histamine and the liberation was dependent on the temperature, *p*H and concentration. Similar observations have been made on liver suspensions in Tyrode buffer solution, and also with sucrose suspensions of particles from sheep-liver capsule, previously shown by Riley and West to consist predominantly of tissue mast cells. The results suggest that histamine is not bound to a tissue component by a primary chemical bond, but most likely enclosed in a diffusible form within a mitochondrion-like particle and histamine can be released by procedures expected to damage a surface membrane. Histamine appears to be mainly located in the mast cells and it is possible that the characteristic granules of these cells contain histamine and they may have a membrane which can be lysed by physical and chemical agents. G. F. S.

Humoral Transmission in the Vagus. C. J. Diaz, P. de la Barreda, A. Molina and R. Alcala. (*Proc. Soc. exp. Biol., N.Y.*, 1954, **86**, 745.) Using dogs linked in cross circulation via the aorta, it is found that a hypertensive substance is obtained on stimulation of the central end of the cut vagus nerve. It is suggested that it is noradrenaline and that it is liberated from the arterial walls. M. M.

Hydrallazine in Hypertension in Pregnancy. F. A. Finnerty. (*Amer. J. med. Sci.*, 1954, **228**, 140.) Hydrallazine by mouth was used as the sole therapeutic agent in 91 pregnant patients with early toxæmia, hypertensive vascular disease or toxæmia superimposed on hypertension. Results were excellent in 36, good in 9, fair in 6, and poor in 40. Therapy was started with a dose of 40 mg. daily (10 mg. 4 times a day after meals and at bedtime) and the dose increased by 40 mg. daily to a maximum daily dose of 400 mg., or until an effective therapeutic result was seen or persistent toxic reaction necessitated discontinuance of the drug or lowering of the dosage. The average effective dosage was 200 to 300 mg. a day; increased dosage failed to enhance the therapeutic effect and doubled the incidence of toxicity. The duration of therapy varied between 3 weeks and 5 months with an average duration of 6·5 weeks. Blood pressure determinations, complete urine analysis, and an ophthalmic examination through dilated pupils (for signs of generalised retinal sheen, indicating early onset of toxæmia) were conducted weekly. Headache was the only major toxic reaction, occurring in 34 patients. A trial of hydrallazine seems indicated in all patients with early toxæmia or progressing diastolic hypertension; if the toxæmic process is not controlled within 2 weeks, the drug should be discontinued. S. L. W.

3-Hydroxy-2-phenylcinchoninic Acid (H.P.C.) in the Treatment of Gout. D. N. Ross. (*Brit. med. J.*, 1954, **2**, 782.) Case reports are given of 12 patients with acute gout or chronic gouty arthritis satisfactorily treated with 3-hydroxy-2-phenylcinchoninic acid. The drug was given in tablets each containing 250 mg. The average daily dose was 1·5 to 2 g. in divided doses with an equal quantity of sodium bicarbonate, after the main meals. Treatment varied from 28 to 270 days. The drug was an effective agent for the treatment of acute gout, and patients treated earlier with colchicine claimed that it relieved their symptoms more quickly and completely. In the chronic type of gouty arthritis its action was slower and less dramatic; about a month's treatment is necessary before improvement occurs, but thereafter acute episodes may be treated or prevented by a few days intensive therapy. The most serious toxic side-effects were skin reactions, which were of an erythematous type in the early stages and were later characterised by vesiculation and sometimes pustulation. The skin lesions cleared on withdrawal of the drug. Except in one case there were no serious renal disturbances, though it would seem wise to have frequent estimations of the blood urea level of any patient receiving medication for a long period. Liver dysfunction was not noted in any of the cases. The author recommends that the drug should be reserved for short-duration treatment of acute gouty episodes or for prophylactic treatment in patients with premonitory symptoms. S. L. W.

3-Hydroxypiperidine, Anticholinergic Activity of Derivatives of. J. P. Long and H. H. Keasling. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 616.) The following tests were used:—dog blood pressure and intestinal contractions (change in sensitivity to acetylcholine), isolated rabbit ileum (inhibition of maximal acetylcholine-induced spasms), rabbit salivation (inhibition of pilocarpine-induced salivation), rabbit eye (corneal reflex, dilatation of pupil and local irritation), rat lacrimation (inhibition of lacrimation induced by β-methacholine chloride and rat (inhibition of passage of a charcoal meal through the intestine). 3-Hydroxypiperidine derivatives were generally more active on the intestinal preparations than on depressor responses, salivation and lacrimation. Quaternisation of the piperidyl nitrogen increased the activity, methyl and ethyl derivatives being about equal in potency. Benzilates were more active than other esters. *N*-Methyl- and *N*-ethyl- 3-hydroxypiperidine methobromides were about as active as atropine. G. B.

Iron Therapy, Intramuscular, in Iron-deficiency Anæmia. I. M. Baird and D. A. Podmore. (*Lancet*, 1954, **267**, 942.) An intramuscular dextran-iron solution was studied for tolerance, absorption, hæmatological response, and reactions. It has the following characteristics: (1) it is about one-third as toxic as iron saccharate solution; (2) it is more stable than iron saccharate both *in vivo* and *in vitro*; (3) it does not precipitate in plasma over a wide *p*H range; (4) it has *p*H of 6·0 to 7·0, is isotonic with tissue fluids, and contains the equivalent of 5 per cent. of iron. The preparation was given by intramuscular injection to 40 patients suffering from iron-deficiency anæmia, and 38 responded adequately to the treatment. The 2 patients who did not respond were subsequently found to be not truly iron-deficient. The total dosage of intramuscular iron given varied between 1000 and 2500 mg., but a mean calculation from the entire series showed that 100 mg. of iron is necessary to raise the Hb 0·34 g./100 ml. The period taken to achieve the maximum rise in Hb was 4 to 9 weeks. The total dose of iron was given in 3 or 4 days to patients in hospital, but out-patients received injections twice weekly with

satisfactory results. After a single intramuscular injection of 4 or 5 ml. serum-iron levels attained a variable peak in 1 or 2 days and returned to about normal after about 6 or 7 days in both anæmic patients and healthy people. There was no evidence of increased urinary excretion of iron after injection of the preparation. The injected iron disappears from the serum more slowly than does saccharated iron oxide. In spite of serum-iron levels as high as 13·8 mg./100 ml. no toxic reactions were observed from the injections. The preparation is concluded to be effective and safe, but should be restricted to iron-deficiency anæmia unresponsive to or intolerant of oral iron where adequate investigation has disclosed no other cause. S. L. W.

6-Mercaptopurine in Leukæmia. J. H. Burchenal, D. A. Karnofsky, M. L. Murphy, R. R. Ellison, M. P. Sykes, C. T. C. Tan, A. C. Memrann, M. Yuceoglu and C. P. Rhoads. (*Amer. J. med. Sci.*, 1954, **228**, 371.) therapeutic activity of this compound was evaluated in 269 patients with neoplastic disease, of whom 140 had acute leukæmia, 8 subacute, 18 chronic myelocytic, and 4 chronic myelocytic leukæmia. Children were given 2·5 mg./kg. by mouth in a single daily dose, with few toxic effects. This dosage is usually tolerated by adults, but bone marrow depression occurred in some. At higher levels severe depression of all formed elements of the marrow was occasionally a serious hazard, but in some adults and children, 5 to 7 mg./kg. was tolerated without difficulty, apart from mild gastro-intestinal disturbances. At 2·5 mg./kg. daily the anti-leukæmic effect of mercaptopurine was not shown until after 3 to 8 weeks of continuous therapy. In 11 out of 12 patients in the early stage of chronic myelocytic lukæmia it produced satisfactory remissions, with a fall in white count, decrease in immature forms, rise in hæmoglobin, and a decrease in splenomegaly and hepatomegaly. A rapid relapse occurred in about 4 weeks in almost all cases when the drug was discontinued, and it is advisable to give maintenance therapy in most cases. Of 87 children with acute leukæmia 41 had good remissions, 16 had partial remissions, and 30 were considered failures. Among the 50 adults with acute leukæmia the results were not so satisfactory, with 7 good clinical and hæmatological remissions, 10 clinical but only partial hæmatological remissions, and 33 failures. The compound had no practical value in chronic lymphocytic leukæmia, lymphosarcoma, Hodgkin's disease, or any of the metastatic carcinomas studied, though slight temporary regressions of tumour masses and subjective improvement were occasionally noted in patients with metastatic reticulum cell sarcoma. S. L. W.

Morphine, Distribution and Fate of, in Dogs and Rats. L. Woods. (*J. Pharmacol.*, 1954, **112**, 158.) Dogs and rats were given doses of morphine and then killed after a specified time and the morphine content of various organs determined. The amount of morphine in the bile, urine and fæces was also estimated. It was found that the spleen, pancreas, thyroid and adrenal contained primarily free morphine while the lungs, liver and kidney contained both free and "bound" morphine. The brain, cerebrospinal fluid and fat contained very little morphine in any form. The main "bound" form of morphine in dog urine and bile is a phenolic substituted morphine mono-glucuronide. Very little difference was found in the tissue distribution between tolerant and non-tolerant animals and the reason for this tolerance is therefore still an open question. M. M.

Morphine, Optimal Dose of. L. Lasagna and H. K. Beecher. (*J. Amer. med. Ass.*, 1954, **156**, 230.) A study of pain relief in 122 patients after operation showed only a slight increase in the potency and duration of analgesia of morphine when the dose was raised from 10 to 15 mg. (The morphine was given in all cases subcutaneously in the form of the phosphate.) The liability of these two doses to cause side-effects and respiratory effects was studied in 10 healthy volunteers. In this latter group a trend was observed towards greater respiratory depression with the larger dose, and a significantly higher incidence of side-effects was recorded. A review of the literature indicates that 15 mg. doses of morphine are probably unnecessary to relieve pain in the majority of patients receiving this drug, and are apparently more likely to produce undesirable side-effects than 8 to 10 mg. doses. In view of these findings the routine use of 15 mg. seems unwarranted, and the optimal dose appears to be 10 mg./70 kg. of bodyweight. S. L. W.

Pentamethonium and Atropine in Paraoxon Poisoning. C. A. de Candole and M. K. McPhail. (*Nature, Lond.*, 1954, **174**, 552.) Evidence is presented to show that pentamethonium bromide significantly increases survival of fully atropinised animals (mice, rabbits and cats) poisoned with paraoxon. A quantitative expression of the therapeutic potency of pentamethonium in mice was obtained by plotting dose-effect curves for intravenous injections of paraoxon, paraoxon with varying doses of atropine, and paraoxon with a full dose of atropine and pentamethonium. The addition of pentamethonium to atropine increased the LD50 over the highest figure obtained with atropine alone by a factor of 2·25. Similar results were obtained with rabbits and cats anæsthetised with a chloralose-urethane mixture and injected with paraoxon so as to cause severe respiratory depression. Only those animals who also received pentamethonium survived. Pentamethonium produced an immediate increase in the respiratory volume, and an initial decrease of blood pressure which was followed by a slow but steady rise. J. B. S.

Plasma, Human, Pain-producing Substance in. D. Armstrong, C. A. Keele, J. B. Jepson and J. W. Stewart. (*Nature, Lond.*, 1954, **174**, 791.) Inflammatory exudates and fresh plasma produce pain when applied to the exposed base of a cantharadin blister and contraction of the isolated rat uterus; both actions being probably due to the same agent which is termed "pain-producing substance". The development of this substance in plasma, which takes 2 to 5 minutes, can be prevented by avoiding contact with glass or metal through using silicone treated needles and syringes, centrifuging in polythene centrifuge tubes and storing in polythene tubes immersed in ice. The substance develops in ten minutes when the plasma is transferred to glass tubes and decays within 1 hour. It has not been possible to isolate the pain-producing substance in a pure form, but its biological and chemical properties resemble those of bradykinin. The substance causes prolonged pain when applied to an exposed blister base, but no itching, flare or wheal. It contracts the rat isolated uterus, which is useful for assay purposes; causes a delayed slow contraction of the guinea-pig ileum; stimulates the rabbit's jejunum and lowers the blood pressure of the cat and the rat. It is stable to acid, but not to alkali. It is a polypeptide, readily distinguishable from serotonin and differs from other biologically active polypeptides such as angiotonin (hypertensin), substance P, leucotaxine, oxytocin and vasopressin, which also produce cutaneous pain and contracts smooth muscle. It is suggested that this substance may be formed when plasma escapes from capillaries and makes contact with damaged tissues. G. F. S.

Rescinnamine, A New Hypotensive and Sedative Principle from *Rauwolfia serpentina*. M. W. Klohs, M. D. Draper and F. Keller. (*J. Amer. chem. Soc.*, 1954, **76**, 2843.) Rescinnamine, the 3 : 4 : 5-trimethoxycinnamic acid ester of methyl reserpate, was isolated by subjecting the benzene soluble portion of the alkaloidal extract from *R. serpentina*, after removal of reserpine by crystallisation from methanol, to chromatographic separation on acid-washed alumina. An amorphous fraction was obtained which readily crystallised from benzene yielding rescinnamine as fine needles, m.pt. 238 to 239° C. (vac.), $[\alpha]_D^{24} - 97 \pm 2$ (*c*, 1·0 in chloroform). Hydrolysis with 0·75N sodium hydroxide in methanol-water yielded reserpic acid and 3 : 4 : 5-trimethoxycinnamic acid. Rescinnamine has hypotensive, bradycardic and sedative activity similar to that of reserpine.

A. H. B.

Reserpine, Hypotensive Action of. E. G. McQueen, A. E. Doyle and F. H. Smirk. (*Nature, Lond.*, 1954, **174**, 1015.) The authors agree with other workers that reserpine diminishes reflex motor responses and they have also demonstrated a direct effect on the peripheral vessels independent of the drug's nervous activity. Using an innervated but otherwise isolated hind limb of a rabbit, perfused with a blood-dextran medium at a constant rate, infusions of reserpine into the systemic circulation produced an immediate fall in blood pressure. This is accompanied by a rise in limb perfusion pressure instead of a fall, as would have been expected were the fall of blood pressure mediated through the nervous system. Furthermore, an immediate diminution in vasomotor tone was caused by injection of the drug directly into the artery of the perfused hind limb. The drug also has a depressant effect on the action of vasopressor substances injected into the isolated rat hindquarter and on the response to nervous stimuli of isolated portions of rat diaphragm. The reactions have a prolonged duration, which suggests binding of the drug by musculature. A direct peripheral effect may also play some part in the hypotensive action of reserpine in man as the blood pressure in the supine position can be brought to a lower level with reserpine plus hexamethonium than by hexamethonium alone.

J. R. F.

Reserpine in the Mentally Ill and Mentally Retarded. R. H. Noce, D. B. Williams and W. Rapaport. (*J. Amer. med. Ass.*, 1954, **156**, 821.) This is a preliminary report on 74 mentally ill and 15 mentally retarded patients treated with reserpine for periods up to 7 months. In both kinds of patient only those were selected who had the worst prognosis and were generally regarded as hopeless; 3 or 4 of the mentally ill patients had received over 100 electroshock treatments. All the patients were given reserpine by mouth in an average daily dose of 2 mg.; in addition many of the patients were given subcutaneous, intramuscular or intravenous injections of up to 10 mg. of reserpine. No alarming reactions followed the injections, except for immediate flushing of the face and extremities after 5 mg. or more intravenously and occasional mild complaints of vertigo or weakness. About 80 per cent. of the psychiatric patients showed marked improvement. Depressed patients became alert and sociable, while the hyperactive, noisy and combative patients became tranquil. The use of restraints, seclusion and electroconvulsive therapy was reduced by at least 80 per cent. Remissions were produced in 20 patients and 8 were discharged. If the results of long-term studies substantially confirm these preliminary findings the authors consider that reserpine will be the most important therapeutic development in the history of psychiatry.

S. L. W.

ABSTRACTS (*continued on page 296.*)