ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

***Veratrum album* L., A New Alkaloid from.** H. R. Hegi and H. Flück. (*Pharm. Acta Helvet.*, 1957, **32**, 57.) This new alkaloid was isolated from the leaf and could not be demonstrated in the subterranean organs. It was separated from the other alkaloids by partition chromatography, and its homogeneity was established by paper chromatography. The melting point, specific rotation and ultra-violet absorbtion characteristics were determined. These latter showed no absorption above 270 mμ, and an ascending curve between 270 mμ and 212 mμ without any maximum, indicating the absence carbonyl groups, α,β-unsaturated carbonyl groups, conjugated double bonds, aromatic rings in an alkamine structure, and unsaturated and aromatic acid components. The reaction with concentrated sulphuric acid was different from that of other veratrum alkaloids. It was concluded to be an ester alkaloid of proposed empirical formula $C_{25}H_{39}O_6N$ (unconfirmed). D. B. C.

ANALYTICAL

Adrenaline, Chormatographic Separation of, from Local Anaesthetics. K. Zachau-Christiansen and J. B. Jensen. (*Dansk Tidsskr. Farm.*, 1957, **31**, 1.) Separation of adrenaline from local anaesthetics (procaine and lignocaine) by the method of Björling is not always satisfactory. The cause has been traced to the use of buffer solutions, which are able to displace adrenaline from alumina. A satisfactory method is as follows: 10 to 20 ml. of a solution containing 50 to 200 μg. of adrenaline plus one drop of methyl red solution is titrated to the neutral point with 0·1N sodium hydroxide. This solution is passed through a column of 2 g. of alumina (Brockmann) in a tube having a diameter of 0·5 cm. After washing with 20 ml. of water, the column is eluted with 30 ml. of 0·1N hydrochloric acid. The eluate is treated with 2·0 ml. of N sodium hydroxide, 2·00 ml. of Folin and Ciocalteau reagent and 8·0 ml. of a 20 per cent aqueous solution of anhydrous sodium carbonate. After making up to 50 ml., and standing for at least 30 minutes, the blue colour is measured at 570 mμ in a 1 cm. cell, after centrifuging if necessary. The solutions used for calibration should contain procaine (or lignocaine) and bisulphite as in the solution to be analysed. G. M.

Aneurine, Determination of, with 6-Aminothymol. K. J. Hayden. (*Analyst*, 1957, **82**, 61.) The rapid photometric method described is suitable for certain pharmaceutical and cereal products and depends upon the intense yellow colour produced on treatment of the vitamin with diazotized 6-aminothymol. The reagent is shown to be more specific than the more widely exploited reagent *p*-amino-acetophenone, and the method is suitable for materials containing upwards of 0·1 mg. of aneurine per g., and the maximum experimental error of a single determination is 1·5 per cent (P = 0·95). D. B. C.

Prednisolone and Prednisone, Determination of. J. Buur Jensen. (*Dansk Tidsskr. Farm.*, 1956, **30**, 293.) A solution containing about 0·3 to 1·0 mg. of the compound in absolute ethanol is treated with 0·5 ml. of semicarbazide acetate reagent, refluxed for 2 hours, and made up to 100 ml. The absorption is then determined at 292 mμ. In the case of tablets the active substance is first extracted by shaking with cold absolute ethanol. The presence of cortisone or hydrocortisone in prednisolone can also be detected by comparison with standards, since the addition of these shifts the maximum absorption from 292 mμ towards lower wavelengths, while the maximum at 242 μ disappears and is substituted by a point of inflection at about 250 mμ. The method has an error which is estimated at about 3 per cent, but it cannot distinguish between prednisolone and prednisone. These two compounds themselves may be distinguished by their melting points and by the solution in sulphuric acid, in which prednisolone gives a wine red colour and prednisone a yellowish green fluorescent solution. G. M.

Rauwolfia Alkaloids, Colorimetric Determination of. H. Wunderlich. (*Pharm. Zentralh.*, 1957, **96**, 68.) After extraction of the medicament with a methanol-acetic acid-water mixture, the solution was cooled to 0° and the alkaloids precipitated by the addition of excess ammonium reineckate after the addition of ether to reduce the solubility of the complex. After filtration, the precipitate was dissolved in methanol and the absorption measured at 427 mμ. Concentrations of about 1 mg./ml. were suitable for constructing a calibration curve, showing that the method is more sensitive than many other methods The author maintains that only by the use of the above solvent in the extraction process, will the alkaloids obtained be fully pharmacologically active. D. B. C.

Sulphonamides, Identification of. H. Baggesgaard Rasmussen, J. Berger and G. Espersen. (*Dansk Tidsskr. Farm.*, 1957, **31**, 66). Sulphonamides were acetylated at the *p*-amino group by boiling the sulphonamide with glacial acetic acid and acetic anhydride for 3 minutes, precipitating by the addition of water and recrystallising from alcohol or glacial acetic acid, followed by drying at 105° for 3 hours. The equivalent weights were determined by titration of the acetyl derivatives with 0·1N lithium methoxide in dimethylformamide, using thymol blue as indicator. The acetyl derivatives did not exhibit sharp melting points, droplets being formed in the capillary tube 10 to 15° below the temperature at which the substance melted completely. The temperature of complete melting was, however, a well-defined character, varying by at most 1 or 2° between determinations. The hydrolysis of sulphonamides was carried out by heating with sulphuric acid or pyrolysis. Pyrolysis required a careful technique and was applicable to only 4 of the sulphonamides investigated. Hydrolysis was best carried out by heating with sulphuric acid (40 per cent) until a precipitate of sulphanilic acid appeared. The liquid was cooled and an excess of sodium hydroxide solution added to dissolve the sulphanilic acid. The amine was extracted with ether, and the extract filtered through exsiccated sodium sulphate, evaporated and dried over silica gel for 24 hours. While the acetyl derivatives were satisfactory for the identification of most of the sulphonamides, the melting points were rather high and in some cases did not provide complete proof of identity. The amines obtained by hydrolysis with sulphuric acid provided a ready means for the identification of all the sulphonamides examined. G. B.

Sympathomimetic Amines, Determination of, by Ion Exchange. M. C. Vincent, E. Krupski and L. Fischer. (*J. Amer. pharm. Ass., Sci. Ed.*, 1957, **46**, 85). Assays of sympathomimetic amines were carried out by adsorbing the amines on columns of ion exchange resins and subsequently eluting them and titrating with acid. For this purpose a strongly basic anion exchange resin (Amberlite IRA–400) gave satisfactory results except with amines containing phenolic groups; these became firmly bound to the resin and could not be recovered under the usual assay conditions. A carboxylic cation exchange resin (Amberlite IRC–50) was satisfactory for the assay of pure amine salts, but not for preparations containing sodium and other ions which were eluted with the amine and interfered in the estimation. This was avoided by the use of a weakly basic anion exchange resin (Amberlite IR–45), which binds weakly both phenolic and non-phenolic amines. Sodium ions and other interfering substances from pharmaceutical preparations can be removed by washing the column with water prior to removal of the amine with ethanol. Quantitative results were obtained by this method using a number of amines. In assaying amines such as adrenaline, which are sensitive to alkali and light it was necessary to protect the column from light and to collect the eluate in 0·1 N hydrochloric acid. The method was successfully applied to a range of pharmaceutical preparations, including capsules, tablets, jellies, inhalers, emulsions and oily solutions. G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Fluorocarbon, Removal of Anticomplementary Activity and Host Antigens from Viral Preparations by. K. Hummeler and V. Hamparian. (*Science*, 1957, **125**, 547.) Fluorocarbon Freon 112 with *n*-heptane to give a solution of s.g. 1·30 (1 part) was mixed with poliomyelitis culture fluid, still containing cell debris (10 parts) and homogenised in a Servall Omnimixer at 14,500 r.p.m. for 3 to 4 minutes, whilst being cooled to 0°. The homogenate was centrifuged at 1000 r.p.m. for 5 to 10 minutes, to separate the aqueous and fluorocarbon layers. The aqueous phase revealed little loss of infectivity, but was free of anticomplementary effects, and specific reactions, not previously evident, were readily apparent. Exposure to fluorocarbons of crude antigens, which were not anticomplementary, caused no decrease of specific reactions. Other tissue-culture antigens (adeno group and Coxsackie B) and antigens derived from chick chorio-allantoic membranes (herpes simplex, mumps soluble antigen) or allantoic fluids (mumps and influenza virus antigens) were similarly treated with fluorocarbon, without loss of antigen titre. J. B. S.

Lysergic Acid Diethylamide, Metabolism of. E. Rothlin. (*Nature, Lond.*, 1956, **178**, 1400.) The report (Axelrod, Brady, Witkop and Evarts (*Nature, Lond.*, 1956, **178**, 143) that little is known of the biological fate of lysergic acid diethylamide, is refuted. It is neither bound nor destroyed in rat blood after incubation for 6 hours at 38°. In the presence of rat tissue homogenates activity decreases within a few minutes, but there is little further decrease thereafter. With liver and muscle homogenates a 50 per cent decrease occurs almost immediately, but there is no further decrease thereafter. With liver and muscle homogenates a 50 per cent decrease occurs rapidly but no further reduction in 17 hours; brain homogenates show 58 per cent reduction in 10 minutes and 79 per cent in 17 hours. Experiments with carbon-14 labelled

lysergic acid diethylamide showed that most organs reached the highest level after 10–15 minutes, but lost it gradually in the course of a few hours, the highest concentration being found in the liver after 30 minutes. Other experiments showed that 7–8 per cent of the activity was excreted within 12 hours, of which about half was in the expired air and the rest in the urine and faeces; 70 per cent was found in the intestinal contents. Labelled diethylamide injected into rats with bile fistula was found in the bile to the extent of 70 per cent within 2 hours. Lysergic acid diethylamide is excreted as water-soluble decomposition products; three substances R_F 0, 0·13 and 0·18 have been separated on paper but not identified. J. B. S.

Purines, Transformation of, into Pteridines. A. Albert. (*Biochem. J.*, 1957, **65**, 124.) The conversion of purines into pteridines has been studied since it is considered that it may shed light on the biological origin of natural pteridines. 2-Hydroxypurine gives 4-amino-5-formamido-2-hydroxy pyrimidine at 20° and pH 5, and 2-mercaptopurine behaves similarly. The formyl group is lost more and more rapidly as it becomes autocatalysed by H^+ ions from the liberated formic acid, giving 4:5-diamino-2-hydroxypyrimidine. The latter combines with glyoxal to give 2-hydroxypteridine in 93 per cent yield at 37° and pH 7. This is typical of a general reaction which proceeds under physiological conditions regardless of substituents in the pyrimidine and requires no catalyst. 1:2-Diketones, aldehydo acids and keto acids react similarly to glyoxal. These reactions are illustrated by a number of examples in which the yields vary from 16 to 85 per cent. Guanine and hypoxanthine undergo similar transformations but less readily. Experiments by Weygand and Waldschmidt (*Angew. Chem.*, 1955, **67**, 328), in which [2-^{14}C]2:4:5-triamino-6-hydroxypyrimidine was fed to pierid caterpillars and [2-^{14}C]xanthopterin was isolated from the wings, support the view that the above reactions are of biological significance. Ziegler and Günder and others (*Z. Naturf.* B., 1956, **11**, 82) found that larvae of the amphibian *Xenopus* similarly were able to convert [2-^{14}C]guanine in labelled pteridine. It is suggested that this reaction may regulate growth in certain circumstances. J. B. S.

CHEMOTHERAPY

Ethyl Mercaptan and Related Compounds. G. E. Davies, G. W. Driver, E. Hoggarth, A. R. Martin, M. F. C. Paige, F. L. Rose and B. R. Wilson. (*Brit. J. Pharmacol.*, 1956, **11**, 351.) In mice infected with *Mycobacterium tuberculosis*, human type strain 905, ethyl mercaptan showed a high activity. Examination of a large number of related compounds has shown that only derivatives that can be metabolized to ethyl mercaptan are active. The ethyl thiol-esters, particularly ethyl thiobenzoate, were most active and found to be superior to other potential sources of ethyl mercaptan. G. F. S.

***Trypanosoma congolense* and *T. vivax*, New Compound Active Against.** W. C. Austin, H. O. J. Collier, M. D. Potter, G. K. A. Smith and E. P. Taylor. (*Nature, Lond.*, 1957, **179**, 143.) Decamethylene bis *iso*quinolinium bromide) (I) and a number of analogues have been prepared and examined for activity in trypanosomiasis. (I) possessed only slight activity against *T. congolense*; a similar order of activity was shown by a series of related polymethylene compounds, activity being at a maximum in this series with hexamethylene bis(*iso* quinolinium bromide). Decamethylene bis(4-aminoquinaldinium iodide) (Dequadin) was appreciably active, and in near lethal doses cured *T. rhodesiense* infections in mice, and also showed prophylactic properties. Dequadin also

possesses high antibacterial and antifungal activity. The primary product of the reaction between 4-aminoquinaldine and hexamethylene di-iodide showed good activity against *T. congolense*, but this was later resolved by fractional crystallisation into three fractions. The most active of these, substance II, was identified by an alternative and unambiguous synthesis as 6′(4-quinaldylamino)hexyl-4-aminoquinaldinium iodide hydrodide. Both the symmetrical isomers hexamethylene bis(4-aminoquinaldinium iodide) (III) and *NN*-bis(4′quinaldyl)-1:6-hexamethylenediamine dihydroiodide (IV) were less active against *T. congolense*, although (III) was slightly more active against *T. rhodesiense*. It is suggested that in general unsymmetrical compounds are more active against *T. congolense*, whilst symmetrical structures have the greater activity against *T. rhodesiense*. Substance II was more active and less toxic than antrycide against *T. congolense* and *T. vivax*. The corresponding chloride to substance II, and its sparingly soluble suramin salt show low toxicity and useful prophylactic activity against *T. congolense*. J. B. S.

PHARMACY

Agar Clarification. J. G. Feinberg. (*Nature, Lond.*, 1956, **178**, 1406.) A simple procedure for agar clarification, adapted from the method Viswanatha and Liener for the purification of a proteinase, is described. New Zealand agar (1 per cent in distilled water) was filtered twice through well rinsed glass wool to remove grossly insoluble particles. At this stage 1 per cent w/v sodium azide may be added as a preservative. A mixture of equal parts of powdered bentonite and 'Hyflo Super Cel' is added (1–2 per cent by volume) and the whole shaken vigorously by hand to disperse the clarifying agents. The suspension is stored at 56° for several days, the clarifying agents being resuspended daily by gentle inversion of the bottles. The clarified agar is decanted and filtered through No. 5 Whatman paper in a hot funnel, the first few ml. being returned for refiltering. The product has the colourless clarity of water in the molten state, and only a faint, clean, unclouded opalescence when set in plates.

J. B. S.

Decanol-1, Solubility of, in Solutions of Sodium Caprate, Laurate and Myristate above the CMC. K. Passinen and P. Ekwall. (*Acta chem. scand.*, 1956, **10**, 1215.) The solubility of decanol in solutions of sodium caprate, laurate and myristate above the critical micelle concentration has been determined, the point of maximum solubility being that at which the solution becomes turbid, due to the separation of a mesomorphic phase composed of decanol, soap and water. The solubility curves are linear over a wide range of concentration above the CMC, before first sloping upwards in a narrow concentration range, and then continuing again as a straight line. The position of the break point in the curves shifts to lower soap concentrations as the molecular weight of the soap increases. The decanol solubility of the mixed micelles decreases with increasing molecular weight of the soap; it is also dependent on the nature of the ionic group in the association colloid and on the gegenions. The meaning of 2nd CMC, and factors responsible for the separation of the mesomorphic phase are discussed. J. B. S.

Decanol-1, Solubility of, in Sodium Oleate Solutions Containing Sodium Chloride. K. Passinen and P. Ekwall. (*Acta chem. scand.*, 1956, **10**, 1228.) The effect of sodium chloride on the solubility of decanol in sodium oleate solutions has been studied, and it has been shown that decanol solubility decreases rapidly with increase of sodium chloride concentration, though the

general shape of the solubility curve is unaltered by sodium chloride concentrations up to 0·05 M. In the presence of sodium chloride the break point in the solubility curve occurs at lower oleate concentrations (0·08 M oleate) than in the absence of salt (at about 0·12 M oleate), though the break is less marked. The solubility of decanol could not be measured when the sodium chloride concentration exceeded about 0·15 M, because solutions become viscous and gel-like. Since the break-point occurs at the so-called 2nd CMC, this must be a function not only of the concentration of the micelle forming hydrocarbon chain ions, but also of the concentration of the gegenions. Factors are discussed, which are responsible for the decrease in the solubility of decanol. J. B. S.

Ferric Saccharate for Injection. J. Büchi and R. Zoppi-Hug. (*Pharm. Acta Helvet.*, 1956, **31**, 497.) The use of colloidal ferric saccharate solution allows the intravenous administration of large quantities of iron and is well tolerated by the patient. A suitable preparation may be made as follows: 18 g. of crystalline sodium carbonate dissolved in 250 ml. of cold water is added in small portions to a solution of 10 g. of ferric chloride in 100 ml. of cold water. The temperature must not exceed 15°. The precipitate is washed free from chloride, and the excess of water is sucked off on a vacuum filter. The fresh ferric hydroxide is rubbed down with 14·5 g. of sucrose plus 0·5 g. of glucose, and a solution of 0·85 g. of sodium hydroxide in 10 ml. of water is added. The mixture is warmed on the water bath until on dilution with 10 parts of water a clear solution is obtained. The liquid is evaporated to dryness on the water bath, and dried at 105°. The solution for injection is prepared by dissolving the preparation in water and adjusting to a content of 2 g. of Fe/100 ml., sterilising through a filter. This preparation does not contain any ions, provided that the pH is not below 7. Its toxicity is low, the LD50 for mice being 150 mg. Fe/kg. G. M.

PHARMACOGNOSY

***Atropa belladonna*, Adulteration of.** M. Wellendorf. (*Dansk Tidsskr. Farm.*, 1956, **30**, 281.) Adulteration of belladonna leaf with *Scopolia carniolica* is difficult to detect in the powdered drug. A useful indication is given by counting the number of idioblasts, containing sandy crystals, per sq. mm. For scopolia this value ranges from about 5 to 8, for belladonna it is about 20. If a value of below 10 is found, then the palisade ratio should be determined as confirmation. This method applies only to the leaf drug; for the herb the results are quite different. G. M.

Saponin in Drugs, Determination of, by Haemolysis. J. Petričić and V. Petričić. (*Acta pharm. Jug.*, 1956, **6**, 95). Extracts were prepared from samples of various saponin-containing drugs grown in Jugoslavia or imported. Although aqueous ethanol was a better solvent than water in some cases, the authors preferred to use aqueous decoctions for the determinations, since the drugs are generally used in the form of aqueous extracts. The addition of sodium bicarbonate did not increase the efficiency of extraction. The saponin content of the extracts was assessed by determination of the degree of haemolysis of citrated cattle blood caused by dilutions prepared in arithmetical progression. A sample of pure saponin was the standard of comparison. On the basis of the results obtained the following are proposed as minimum standards for the Jugoslavian Pharmacopoeia: herniary herb 30, primula root 120, quillaia bark 75, saponaria root 50 and senega root 75 units per g. The Ph. Jug. unit is equivalent to 1 mg. of the standard saponin sample. G. B.

PHARMACOLOGY AND THERAPEUTICS

Antifoam Agents in Pulmonary Oedema. R. C. Balagot, R. M. Reyes and M. S. Sadove. (*J. Amer. med. Ass.*, 1957, **163**, 630.) A new compound, No. 5507, which consisted of silicone 0·01 per cent, Superinone (a polyhydric alcohol) 0·75 per cent, glycerol 1 per cent, and potassium bicarbonate 1 per cent, was tested for its ability to suppress foam in adrenaline-induced pulmonary oedema in rabbits. It was compared with octyl alcohol, and 10 and 20 per cent ethanol and was found much superior to any of these, giving a survival rate (in 24 rabbits) of 53 per cent; it also compared favourably with results previously obtained (Luisada and Cardi) with 95 per cent ethanol. Animal studies showed the compound to be non-toxic and to have no depressant effects on the central nervous system. Clinically, excellent results were obtained in 8 patients with pulmonary oedema, there was almost immediate suppression of foam, the oedema quickly cleared, and the cyanotic condition of the patients improved. S. L. W.

β-Diethylaminoethylphenothiazine-10-carboxylate Hydrochloride (Transergan), Studies on. S. Wiedling. (*Acta. pharm. tox. Kbh.*, 1957, **13**, 59.) This is a new phenothiazine derivative which has been found to be valuable clinically as a non-specific spasmolytic and antiparkinsonism. It has a strong spasmolytic action against spasms induced in isolated tissues by acetylcholine, histamine, 5-HT and barium, but against adrenaline and noradrenaline its action is weaker. It has a strong local anaesthetic action on the eye, being about five times as active as lignocaine, but it also has a local irritant action. Intravenously it does not potentiate the local anaesthetic action of lignocaine and it is considered therefore to have no central analgesic action. Doses of 1 mg./kg. or over reduce the rabbits blood pressure, but it does not antagonise the actions of acetylcholine, histamine, adrenaline or noradrenaline. Only with toxic doses (10 mg./kg.) is there a noticeable reduction of the body temperature of the rabbit. The acute LD50's to mice were oral 0·44 g./kg., subcutaneous 0·62 g./kg., intraperitoneal 0·14 g./kg. and intravenous 0·027 g./kg. Toxic doses cause tonic and clonic convulsions, while lower doses have a sedative effect preceded by a stage of excitation, irregular respiration and Straub phenomena. The chronic administration of doses up to 30 mg./kg. daily over one month does not reduce the growth of rats and produces no pathological effects. Against a haemolytic strain of *Staphyloccus aureus* a concentration of 4×10^{-4} has a bacteriostatic effect and 8×10^{-4} a bactericidal effect.

G. F. S.

Ganglion-blocking Activity of a Series of 4-Aminoethylpiperidine Derivatives. K. I. Colville and R. V. Fanelli. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 727.) A series of derivatives of 4-β-aminoethylpiperidine of the general formula $XRR'N{\cdot}C_5{\cdot}H_9{\cdot}CH_2{\cdot}CH_2{\cdot}NR''R''RX$ was examined. The compounds were tested for hypotensive activity in anaesthetised cats and for ganglion-blocking action using the nictitating membrane of the anaesthetised cat. The LD50 was determined in mice. The most potent compound examined was R′=Me,R″R″′N=pyrrolidino,R=Et,X=I, and the analogous compound where R=Me was slightly less potent. The corresponding tertiary amines were found to be much less active than their quaternary derivatives. The hypotensive action appeared to be almost entirely due to the ganglion-blocking activity of the compounds. The effect of varying the substituent groups is discussed. G. B.

Glutethimide in Labour. T. M. Abbas. (*Brit. med. J.*, 1957, **1**, 563.) This study is based on a survey of 100 parturient patients, consisting of equal numbers of primiparae and multiparae, given two tablets of glutethimide (each containing 250 mg.) early in the first stage of labour. For control purposes a second series of 100 cases of normal parturient patients were treated with 30 grains of chloral hydrate as a syrup. In the glutethimide group good relief of pain was obtained in 70 of the patients, fair relief in 12, and poor relief in 18. Mental and physical relaxation, with ability to sleep between contractions, was good in 72, fair in 10, and poor in 18. In the glutethimide group the average length of labour was 12 hours for primiparae and 7½ hours for multiparae; in the control series the corresponding figures were 13½ and 8 hours. There were no maternal or foetal deaths and no significant untoward effects attributable to the drug. Four patients had nausea and 5 vomited within 3 hours of administration of glutethimide. In the chloral hydrate group vomiting occurred in 77 patients. The total amount of pethidine needed for additional sedation and analgesia in the glutethimide group was substantially less than that required in the control series. Glutethimide was well tolerated by all patients, and none showed any allergic reaction. There was no significant difference in the incidence of post-partum haemorrhage in the two groups. All patients who initially were apprehensive lost their fear and became fully cooperative shortly after administration of the drug, greatly facilitating the general management of the first stage. S. L. W.

Lead Poisoning, Treatment of, with Calcium Edetate. O. Wegelius and A. Harjanne. (*Scand. J. clin. lab. Invest.*, 1956, **8**, 335.) A series of 5 patients, 3 with acute lead poisoning and 2 with mild subjective symptoms and definite signs of lead poisoning were given daily intravenous infusions of 2·5 g. of calcium edetate in 1000 ml. of 5 per cent dextrose solution for a period of 10 days. For those patients with the more severe symptoms, the treatment was repeated after an interval of one week. Urinary excretion of lead increased greatly during the treatment, and in all cases nausea, cramping abdominal pains, fatigue and any anaemia present disappeared, and no basophilic stippling of the red cells was visible. The urinary coproporphyrin returned to the normal level. No untoward effects, such as renal damage were observed at the dosage level employed, although they have been reported when larger doses of calcium edetate were given. G. B.

Methylpentynol; Toxic Effects and Side-Effects. E. Marley and J. S. W. Chambers. (*Brit. med. J.*, 1956, **2**, 1467.) Eight case histories of toxic reactions to methylpentynol given in therapeutic dosage are described. The physical signs included pupillary abnormalities, nystagmus, diplopia, ptosis, loss of facial muscle tone, dysarthria, tremor of the protruded tongue, and cerebellar ataxy in the limbs or admixtures of this with posterior column ataxia. Muscular tone was usually diminished. Plantar reflexes were flexor and sensation remained unaffected. Mood change, particularly depression, dominated the accompanying mental state in these patients. Disorientation was not observed, but nominal dysphasia, paraphasia, distortion of subjective time experience and body image were noted. Illusions or hallucinations were common, as was impairment of memory for the toxic episode. Withdrawal symptoms were seen in one patient who had been taking from 1 to 1·5 g. of methylpentynol daily for 10 months. In addition to the foregoing, side-effects (as distinct from toxic phenomena) were noted in two groups, each of 15 patients, the one given therapeutic doses (0·5 to 2 g. a day) for 1 to 6 weeks, and the other

receiving larger doses (about 5 g.) during labour. Side-effects on these two groups were confined to minor alterations in the mental state; dizziness and light-headedness were the most frequent side-effects noted. The authors emphasise the resemblance to barbiturate or alcoholic intoxications, and also the small doses and brief duration of action which may precipitate toxic reactions, especially in patients with psychiatric disorders. S. L. W.

Methyprylone, Clinical Trial of. J. S. Stewart. (*Brit. med. J.*, 1956, **2**, 1465.) A controlled trial was carried out on 100 patients in the ear, nose and throat wards of a London hospital to compare the hypnotic effect of methyprylone with amylobarbitone sodium and butobarbitone. Four sets of tablets identical in appearance and closely similar in taste were prepared: amylobarbitone sodium 100 mg., butobarbitone 100 mg., methyprylone 200 mg., and a control (lactose, starch, and a trace of infusion of quassia). One of the tablets was given on each of four consecutive nights, and the results assessed objectively by the nursing staff (speed of onset and duration of action) and subjectively by the patients (speed of onset, quality of sleep, and nature of after-effects). The results showed no significant difference between the mean scores for the three drugs. The score for the control was not greatly lower but was statistically significant. The only side-effect recorded was headache which occurred twice after each drug and once after the control. The author concludes that methyprylone is a reliable non-barbiturate hypnotic of comparable effect to amylobarbitone sodium and butobarbitone. S. L. W.

Noradrenaline in Shock Due to Visceral Perforation. D. D. Davies. (*Brit. med. J.*, 1957, **1**, 261.) Three cases are described in which noradrenaline had to be used to maintain adequate blood pressure after traditional methods of resuscitation had failed. Two patients with perforation of the large bowel recovered completely; the third patient, with peptic ulcer perforation, showed a good immediate recovery but died 12 hours later from a pulmonary embolus. The noradrenaline was given by intravenous infusion, commencing with a strength of 8 mg. of noradrenaline per 1000 ml. of dextrose-saline, the strength being increased to 16 mg. and later to 32 mg. per 1000 ml., and the drip-rate varying between 25 and 80 drops per minute. The strength of the solution and the rate of drip were adjusted throughout to raise and maintain the systolic pressure at about 90 mm. Hg or above. In the treatment of shock due to visceral perforation simple infusions of blood or dextran alone are usually effective in permanently maintaining an adequate blood pressure level provided that the factors causing the shock are effectively treated. In these cases infusions of blood or dextran should therefore first be instituted, but if these measures fail then the early use of continuous noradrenaline infusion holds out the best chance of recovery. Its early use in the shocked state probably produces an increase in blood flow to vital organs. This and the correction of the myocardial ischaemia, following the increase in coronary blood flow, may be important factors in helping to prevent the development of an irreversible phase in which noradrenaline therapy is of no avail and may do more harm than good. The author stresses the paramount importance of adequate oxygenation in the shocked patient. S. L. W.

Nystatin in Moniliasis. E. T. Wright, J. H. Graham and T. H. Sternberg. (*J. Amer. med. Ass.*, 1957, **163**, 92.) Nystatin was used topically in the treatment of 122 patients with infections due to *Candida albicans*. There were 42 patients with oral moniliasis, 17 with vaginal moniliasis, and 63 with such cutaneous

involvement as paronychia, intertrigo, and perlèche. Nystatin was applied in the form of ointments, solutions, powders, troches, capsules, suppositories and jelly for vaginal use. The ointment and gel consisted of a plasticised petrolatum base containing 5,000 to 200,000 units/g. of Nystatin. Two types of solution, containing 5,000 and 100,000 units/ml. were used; one was propylene glycol solution, and the other contained 2 per cent procaine hydrochloride and 0·25 per cent polysorbate 80. The latter solution was prepared both with and without 2·5 mg./ml. of hydrocortisone. The powder contained 175,000 units of nystatin per teaspoon. The troches contained 200,000 units, and in addition some contained 2·5 mg. of neomycin sulphate and 0·25 mg. of gramicidin. The capsules and tablets used as troches and suppositories contained 125,000 to 500,000 units of Nystatin. The suppositories contained 10,000 to 100,000 units. The cutaneous infections were treated with ointments and solutions 4 times daily. Oral infections were treated with solutions, troches, capsules and tablets used as troches 4 times daily. In addition the powder was used orally 4 times daily (one teaspoonful in glass of milk or water as a mouthwash). Vaginal infections were treated once daily with the use of disposable applicators, suppositories, and tablets and capsules used as suppositories. Treatment periods varied from 3 days to 1 month. In all but 5 cases the response to treatment was good to excellent. The lesions ordinarily disappeared in 2 or 3 days in thrush or perlèche, though some patients required 2 or 3 weeks. Clinical relapses were infrequent, though in 43 per cent of the patients repeat cultures revealed the presence of *C. albicans* even though the lesions had disappeared. This was especially true in patients with severe systemic diseases, especially diabetes. The type of vehicle in which the Nystatin was placed influenced the clinical effectiveness. Solutions were more effective in intertriginous areas. The addition of hydrocortisone to the solution shortened the course of therapy.

S. L. W.

APPLIED BACTERIOLOGY

Lactobacilli and Streptococci, Differentiation of, by Paper Partition Chromatography. A. T. R. Mattick, G. C. Cheeseman, N. J. Berridge and V. Bottazzi. (*J. appl. Bact.*, 1956, **19**, 310.) This is a report of the application of 2-dimensional paper partition chromatography of extracts of washed bacterial cells to the differentiation of species of *Lactobacillus* and *Streptococcus*. Preliminary experiments revealed that application of bacterial cells directly to the paper yielded chromatograms full of faint streaks. Delayed extraction of soluble material was held to be responsible for this streaking. The method afterwards adopted consisted of preparing a suspension from a 24 hour culture of the organisms, adjusting the suspension to a definite optical density, and washing the cells twice by centrifuging and resuspending in standardised volumes of water. Finally the cells were suspended in 10 per cent v/v acetic acid. The suspension was allowed to stand for 4 hours, centrifuged and drops of the supernatant spotted on to the chromatogram paper. The chromatogram was developed first with butanol-acetic acid and then with *m*-cresol and phenol for the second dimension. Results were recorded as widths and lengths of spots and as R_F values relative to the position of alanine. The positions were recorded with the aid of an "adjustable shadowgraph" which is described in detail. The results indicated that the patterns of amino acids and peptides revealed by ninhydrin were generally constant for closely related strains within a species. Variations were found with different species, some being otherwise difficult to