ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Codeine, Narcotine and Thebaine, Determination of, in Poppy Capsules. J. Holubek, S. Kudrnác and M. Novák. (*Die Pharmazie*, 1958, **13**, 95.) In this method, codeine and narcotine are separated from the other opium alkaloids by paper chromatography. Codeine is then determined colorimetrically by oxidation with potassium permanganate, removal of excess with ferrous ammonium sulphate, treatment with alkali to remove the iron, and colour development with equal parts of diazo reagents I and II of the *Deutsche Artzeneibuch*, 6th edition. It is shown that narcine, which could not be separated from codeine by paper chromatography, did not interfere. In amounts between 50 and 200 μg., the results are within ± 2 per cent. Narcotine is determined after elution from the paper by hydrolysis to cotarnine with dilute sulphuric acid, followed by polarography in alkaline solution. In amounts between 50 and 200 μg., the results are within ± 4 per cent. Full details are given for the preparation and purification of the extract, and the results are tested by the addition of known amounts of codeine and narcotine to assayed extracts and redetermination. Very good agreement is obtained. The assay of thebaine after elution from the filter paper was however not satisfactory. The method given is a direct colorimetric one based on hydrolysis in acid solution to codeinone and coupling with diazotised sulphanilic acid. Excess of codeine, narcotine and papavarine did not interfere. The method is suitable for amounts up to 100 μg. of thebaine. The soundness of this method was again proved by addition of known amounts of thebaine to assayed extracts and reassay.

D. B. C.

Cycloserine and Isoniazid, Spectrometric Determination of, in Pharmaceutical Preparations. J. M. Woodside, I. Piper and J. B. Leary. (*J. Amer. pharm. Ass., Sci. Ed.*, 1957, **46**, 729.) Pharmaceutical preparations of cycloserine may be assayed by measurement of the ultra-violet absorption of a suitable solution in 0·1 N hydrochloric acid at 219 mμ, calculating the cycloserine content from the datum $A_{219m\mu} = 0{\cdot}341$ for a solution containing 10 μg. of cycloserine per ml. When isoniazid is present in addition to cycloserine, a further measurement is made at 272 mμ. Cycloserine does not absorb at this wavelength, and the isoniazid content may be calculated directly. To allow for the absorption at 219 mμ due to isoniazid, the absorption at 272 mμ, multiplied by 1·13 is subtracted from the absorption at 219 mμ before calculating the cycloserine content of the sample.

G. B.

***n*-Butanol as a Standard of Haemolytic Index.** J. Vandeputte-Poma and R. Ruyssen. (*Pharm. Weekbl.*, 1958, **93**, 94.) As a standard of comparison for the determination of haemolytic index, *n*-butanol is preferable to other substances such as saponins, because it is less variable in composition. The authors report a detailed study of haemolysis by *n*-butanol with a view to its use as a standard. A method of assay based on comparison of the concentration of sample and standard causing 50 per cent haemolysis of a suspension of erythrocytes is recommended.

G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

2-Methoxyoestrone, a new Metabolite of Oestradiol-17β in Man. S. Kraychy and T. F. Gallagher. (*J. biol. Chem.*, 1957, **229**, 519.) After the administration of oestradiol-17β-16-^{14}C to human subjects, 2-methoxyoestrone was isolated from the urine. The structure of this compound was established by synthesis. It is suggested that this steroid, a methylated *o*-hydroquinone, is a normal metabolite of the oestrogenic hormone. The significance of this is that oxidation of the aromatic ring is achieved under *in vivo* conditions and probably this is a preliminary stage to fission of the carbon skeleton. In this respect the reaction would be similar to the *in vivo* formation of 3:4-dihydroxyphenylalanine from tyrosine. It is also of interest that this is a reaction involving the methylation of oxygen, perhaps similar to the *O*-methylation *in vivo* of 3:4-dihydroxymandelic acid, a metabolite of noradrenaline in man. That two such aromatic hormones are similarly altered emphasises the endocrine significance of this type of biochemical transformation. This work suggests that the metabolism of oestrone or oestradiol is accomplished in two separate stages; firstly oxidation and subsequently methylation. M. M.

Nalorphine, Inhibitory Action of, on the Enzymatic *N*-Demethylation of Narcotic Drugs. J. Axelrod and J. Cochin. (*J. Pharmacol.*, 1957, **121**, 107.) It has been shown that a variety of narcotic drugs are *N*-demethylated by an enzyme system found in mammalian liver microsomes. Since nalorphine blocks the pharmacological action of the same compounds that are attacked by this enzyme system a study is made to determine whether or not its inhibitory action extends to the process of *N*-demethylation. The degree of *N*-demethylation in rat liver enzyme preparations incubated with morphine alone and combinations of morphine with varying amounts of nalorphine, was determined. Marked inhibition of morphine demethylation, directly related to the nalorphine concentration, was observed. It appears that this inhibition is non-competitive but it is possible that it is a slow pseudo-irreversible inhibition mimicking non-competitive inhibition but occurring at the same site. Studying a series of narcotic drugs, it was found that, with the exception of cocaine, the *N*-demethylation of such substances was inhibited by nalorphine. There was greater inhibition of the demethylation in compounds in which the methyl group is attached to the nitrogen atom of the piperidine ring. The effect of nalorphine on other pathways of drug metabolism was also investigated. Nalorphine blocked the enzymatic *O*-demethylation of codeine but had no effect on the *O*-demethylation of *p*-methoxybenzonitrile. The enzymatic de-esterification of pethidine was not blocked by nalorphine and the side-chain oxidation of hexobarbitone was inhibited only slightly. Studying analogues of nalorphine, it was found that, with the exception of *N*-propyl*nor*morphine, *N*-substituted *nor*morphine derivatives with a 3-carbon chain linked to the nitrogen atom are the most potent inhibitors. Nalorphine was found to be dealkylated to *nor*morphine by enzymes in the rat liver microsomes when incubated with the soluble supernatant fraction of rat liver, triphosphopyridine nucleotide and nicotinamide. The rate of dealkylation of nalorphine was more than twice that of morphine. M. M.

BIOCHEMICAL ANALYSIS

Acetylcholinesterase Activity, Colorimetric Determination of. D. N. Kramer and R. M. Gamson. (*Analyt. Chem.*, 1958, **30**, 251.) This depends on hydrolysis by the enzyme at pH 8·0 of indophenyl acetate (*N*-4′-acetoxyphenyl)-*p*-quinone imine which is reddish yellow to the blue-purple *p*-quinone imine *N*-4′-phenoxide ion. A blank determination is performed and the absorbance of the hydrolysis product is measured at 625 mμ after a definite time, normally 15 minutes but may be extended to two hours for weak solutions of the enzyme. The method is precise and reproducible in the range of 25 to 150 units of acetylcholinesterase. The effect of variables such as pH, substrate concentration, time, stability of reagents and the effects of alcohol, albumin and hydrolysis product is discussed. D. B. C.

Parathion, Detection and Quantitative Determination of, in Biological Materials. K. Erne. (*Acta pharm. tox., Kbh.*, 1958, **14**, 173.) A specific and sensitive method is described for the identification and quantitative determination of parathion and *p*-nitrophenol in biological material. Acidify 10 g. of the homogenised sample with 1 ml. of 5 M sulphuric acid, triturate with 20 g. of Hyflo Supercel and extract with benzene in a Soxhlet for four hours. Concentrate in a current of air to 25 ml., filter and chromatograph the solution on an alumina column. Elute the parathion with ether and the *p*-nitrophenol with methanol. The parathion is analysed by paper chromatography developed with *iso*-octane saturated with dimethyl sulphoxide. It is identified by a yellow band at R_F 0·7 formed by spraying the dried paper with 0·5 M ethanolic potassium hydroxide followed by heating at 100° for 5 minutes. A quantitative determination is made by excising this area from another strip of paper prepared in the same way. This is extracted by suspending the paper in a condenser and refluxing into a small flask with ethanol. Add through the condenser 4 drops of 5 M hydrochloric acid, 3 ml. of water and one granule of zinc and reflux for ten minutes. Transfer the liquid to a 10 ml. volumetric flask, and add at four minute intervals 4 drops of 0·25 per cent sodium nitrite, 2·5 per cent ammonium sulphamate and 1 per cent naphthyl ethylenediamine solutions. Add water to 10 ml. and thirty minutes later read the extinction at 555 mμ against a blank. Compare with a standard parathion calibration curve prepared the same way. The *p*-nitrophenol is determined in the methanol eluate evaporated to 10 ml. Add 1 ml. of 5 M sodium hydroxide, 50 ml. of water and extract the lipids with ether. Acidify, extract with ether, wash the extracts with 25 per cent sodium sulphate, dry with anhydrous sodium sulphate, wash with ether and adjust the volume to 0·4 ml. with methanol. Carry out paper chromatography developed with *n*-butanol saturated with 5 M ammonia. Air-dry the paper, and a yellow band at R_F 0·5 indicates the presence of *p*-nitrophenol. For quantitative estimation eluate the excised yellow band by refluxing with methanol as before. To the solution add 1 drop of 5 M sodium hydroxide and methanol to 10 ml. Read the extinction in the 350 to 450 mμ region. Compare with a standard curve prepared in the same way. G. F. S.

Tolbutamide, Determination of, in Serum. E. Bladh and Å. Nordén. (*Acta pharm. tox. Kbh.*, 1958, **14**, 188.) A method is described for determining tolbutamide based on Forist's method of chloroform extraction and ultra-violet measurement at 228 mμ. Mix one ml. of serum with 1 ml. of water and 1 ml. of 6 N hydrochloric acid. Shake for 15 minutes with 20 ml. of chloroform, separate and wash with 2 ml. of chloroform. Pass the chloroform solutions containing the tolbutamide through a chromatography tube packed

with calcium carbonate or sodium bicarbonate and evaporate under reduced pressure at 30° in a flask. Add 10 ml. of absolute ethanol to dissolve the residue and measure the absorbancy of the solution in a spectrophotometer at 228 mμ. A serum sample without the tolbutamide is carried through the same procedure as the blank. The serum concentration of tolbutamide is determined from a standard curve, and the accuracy of the method is ±0·6 mg. per cent. The method may be improved by buffering the plasma to pH 4·5 to 4·8 before chloroform extraction. Recently Spingler (*Klin. Wschr.*, 1957, **35**, 533) has introduced a colorimetric method, which makes use of the formation of butylamide when tolbutamide in an inert solution medium is exposed to increased temperature. Butylamine gives a yellow colour with dinitrochlorbenzene or dinitrofluorbenzene. G. F. S.

Vitamin B_{12} in Natural Materials of low Potency, Estimation of. J. M. McLaughlan, C. G. Rogers, E. J. Middleton and J. A. Campbell. (*Canad. J. Biochem. Physiol.*, 1958, **36**, 195.) Existing methods for the estimation of vitamin B_{12} in low potency materials frequently lack specificity and often are subject to considerable variation. The *Lactobacillus leichmanii* assay for vitamin B_{12} does not give reliable results in the presence of desoxyribosides and certain of the vitamin B_{12}-like factors to which *L. leichmanii* responds. A radioactive tracer assay which is specific for vitamin B_{12}, and which has been adopted by the U.S.P., is not applicable to materials of low potency because of the necessity of measuring the vitamin spectrophotometrically. This paper describes the modification of the method so that it is suitable for low potency materials. The purification procedure is effective in removing pseudovitamin B_{12} and factor A but is ineffective in removing vitamin B_{12} III. A correction factor is used in place of ^{60}Co-labelled vitamin B_{12} to adjust for loss during purification. This purification does not affect the estimates of vitamin B_{12} activity of milk, plasma, chick mash, or fish meal. True vitamin B_{12} activity is apparently responsible for 50 per cent of the total vitamin B_{12} activity of dried cattle faeces and for less than 10 per cent of the total activity of yeast activity. The coefficient of variation of the modified method was 8·7 per cent based on 20 estimates of potency. M. M.

PHARMACY

Adrenaline and Noradrenaline, The Stability of Injections of. J. Mørch. (*Pharm. Weekbl.*, 1958, **93**, 141.) Decomposition was assessed by determinations of biological activity in rats. The injection solutions of the Danish Pharmacopoeia were investigated; they contained 0·1 per cent of adrenaline with hydrochloric acid or 0·01 per cent of noradrenaline as bitartrate, and the solutions were prepared using water redistilled in glass, containing 0·05 per cent of sodium metabisulphite (pyrosulphite). The solutions before autoclaving had a pH of 3 or 4, which decreased to 2·9 or 3·4 owing to the oxidation of metabisulphite to sulphuric acid during sterilisation. Solutions of adrenaline lost about 4 per cent of their activity during autoclaving at 120° for 20 minutes, and noradrenaline solutions lost only 2 per cent. All solutions remained colourless after this treatment. On heating at 100° for 27 hours, the solutions were little affected by the presence of 2 μg. of copper ion per ml., but considerable decomposition occurred in the presence of 20 μg./ml. During storage at 100°, oxidation occurred slowly at first, the observed loss in activity being mainly due to racemisation. Later, as the metabisulphite was destroyed, the oxidation

took place more rapidly, and finally more slowly as the oxygen in the container was used up. The presence of metabisulphite prevented discoloration, but even when it was added in excess compared with the oxygen content of the ampoule it did not completely prevent the decomposition of adrenaline or noradrenaline.

G. B.

Adrenaline, Oxidation of, *In Vitro*, by Copper in the Presence of Plasma and Plasma Fractions. P. Varène. (*Bull. Soc. Chim. Biol.*, 1957, **39**, 1473.) The decomposition of adrenaline in solution in the presence of copper ions was assessed biologically and colorimetrically as described previously (see abstract *J. Pharm. Pharmacol.*, 1958, **10**, 332). The reaction was considerably retarded by the addition of heparinised plasma to the solution. The albumin fraction had the greatest retarding effect, and protected the adrenaline as effectively as a quantity of plasma containing the same weight of proteins. The globulins were inactive, and the dialysable fraction showed only a slight effect, which was attributed to its amino acid content. There appears to be no simple protective mechanism, but if it is assumed that the catalyst can become partly attached to the protein, it seems that the adrenaline must also form bonds with proteins.

G. B.

Bacteriostatics For Parenteral Injections of Procaine Penicillin. C. L. Sargent. (*Pharm. Weekbl.*, 1958, **93**, 81.) Solutions containing 50,000 to 500,000 units/ml. prepared from penicillin admixed with 4 per cent of sodium citrate were shown to retain their original potency for at least 8 days when stored at 4°. At 25°, solutions containing 100,000 units/ml. were stable for 4 days if made from penicillin-citrate mixture containing 4 or 5 per cent of sodium citrate, but not if made from a mixture containing 3 per cent of citrate. Stronger solutions, containing 500,000 units/ml. were less stable and did not retain their potency for 4 days at 25° when made from a mixture containing 4 or 5 per cent of citrate. Deterioration of the solutions was not invariably accompanied by obvious physical change. An attempt was made to find an antiseptic which would confer on procaine penicillin suspensions about the same bacteriostatic power as 0·5 per cent phenol solution. Phenylmercuric nitrate 0·001 per cent and propyl hydroxybenzoate 0·02 per cent with methyl hydroxybenzoate 0·2 per cent were rejected as ineffective; moreover in the presence of the hydroxybenzoates a precipitate tended to form in 5 to 7 days. Benzyl alcohol 1·5 per cent and phenol 0·5 per cent showed a satisfactory bacteriostatic effect, but rendered the suspensions viscous after a few days' storage and afterwards caused the development of a yellow colour. Cetrimide 0·01 per cent was the most satisfactory bacteriostatic agent examined, but adsorption onto the medicament occurred, and the whole suspension had a greater bactericidal effect than the supernatant liquid. Samples of cetrimide from several sources varied in bactericidal potency, and it is suggested that a minimum amount should be specified.

G. B.

Cod Livers, Investigation of the Oil Obtained by a Freezing Procedure from. S. Erbe, (*Arch. Pharm.*, 1958, **28**, 1.) The following freezing process for the extraction of the liver oil is said to give a product of higher vitamin activity and pleasanter taste than those obtained using superheated steam:—The fresh livers are slowly frozen so that large ice crystals form in the cells. Temperatures down to −50° are used. Rapid freezing causes the formation of small crystals so that the cells are not completely disrupted in the subsequent grinding process, resulting in loss of oil. After fine mincing and thawing in the absence of air as far as possible, the oil is separated by centrifuging. The taste of such an

oil is only weakly fishy and the oil will keep four to five months at 3–5° before a slight alteration in taste is noticed. It is important, however, not to allow the livers to remain in a frozen condition for too long, since even after a few days the acid value rises appreciably, probably due to the activity of tissue lipases which remain active at temperatures as low as −25° to −30°. D. B. C.

Solutions Varying From the Normal Osmotic Pressure and Hydrogen Ion Concentration, Sensitivity of the Human Eye to. C. Trolle-Lassen. (*Pharm. Weekbl.*, 1958, **93**, 148.) Healthy individuals were used for the tests. A non-irritant solution was instilled into one eye, and the test solution into the other. The experiment was repeated with other strengths of solution and from the results the threshold of irritation was calculated. Considerable variation was observed in the sensitivity of individuals to solutions diverging from the normal osmotic pressure and hydrogen ion concentration of the lachrymal fluid, which corresponds to a freezing point depression of 0·52° and a pH of 7·4. Solutions causing irritation in 1 per cent or less of the individuals used in the tests were considered to be non-irritant. Using this criterion solutions of freezing point depression 0·41° to 0·77° (equivalent to 0·7 to 1·4 per cent of sodium chloride) and pH 7·3 to 9·7 were classified as non-irritant. Thus the eye tolerates hypertonic rather than hypotonic, and alkaline rather than acid solutions. It was observed that substances such as urea, although they pass freely through animal membranes, affect the osmotic pressure of solutions for instillation, and should be taken into account in adjusting the freezing point of solutions for use as eye-drops. G. B.

PHARMACOGNOSY

***Salvia officinalis* L., Periodical Daily Variations in the Content of Volatile Oil in the Leaves of.** R. Schib. (*Pharm. Acta Helvet.*, 1958, **33**, 32.) This investigation shows that the volatile oil content of *Salvia officinalis* has significant and regularly repeated variations during a 24-hour period. Thus it was found that the maximum content occurred between noon and 4 p.m., and the minimum between 11 p.m. and the early hours of the morning. The difference between maximum and minimum contents, referred to the crude fibre (since this was the least variable factor) was found to be between 34 and 45 per cent of the minimum content. In fully developed leaves the curves oscillated between maxima and minima, whereas very young plants showed a small secondary maximum between 1 and 5 a.m. The curves of the diurnal variations were found to be approximately parallel with those of air temperature. Collections were made at 4-hourly intervals. In order to minimise the sources of error which occur in the investigation of daily variations of phytochemical processes, leaves of as far as possible the same age and size were gathered from the same plant, preferably from the same height of insertion. A further series of investigations was made on seedlings from uniform seed which showed the first three leaf pairs, leaves from different plants being collected. At each collection climatic conditions were noted, e.g. temperature, wind, sunshine and the official figure for the relative humidity. The leaves were immediately wrapped in gauze and dried for 2 days in a closed tin containing lime. The variations were referred to fresh weight, dry weight and to weight of fibre, and all results showed the same trend, while those based on weight of crude fibre were considered to be least affected by other variables. The oil was determined by an oxidation method having a scatter of only ±0·5 per cent. D. B. C.

PHARMACOLOGY AND THERAPEUTICS

Azacyclonol in the treatment of Schizophrenia. S. Gray and A. D. Forrest. (*Brit. med. J.*, 1958, **1**, 374.) From a controlled trial of azacyclonol in 40 chronic schizophrenic patients it would appear that the drug is unlikely to prove of great value in the treatment of this type of patient. Better results, however, were obtained in 18 patients whose illness was of more recent onset; 13 of the patients improved and 6 were discharged from hospital. It is suggested that azacyclonol has a central stimulant action and part of the poor results in the controlled trial may have been due to the masking effects of excitement and over-activity which made the patients' mental disturbance more obvious during the interview. Also the dosage in the controlled trial was less, 60 mg. daily, as compared with a range of 60 to 180 mg. daily in the clinical trial. S. L. W.

Bemegride, Further Aspects of the Analeptic Activity of. A. Shulman and G. M. Laycock. (*Aust. J. exp. Biol. med. Sci.*, 1957, **35**, 421.) It is already known that bemegride (β-methyl-β-ethylglutarimide) is an effective antagonist to narcosis induced by a wide variety of barbiturates and by substances structurally related to the barbiturates such as 2:4-diketothiazolidine,5-phenyl-2:4-diketothiazolodine, the monoureides bromural and carbromal, and β-methyl-β-(butyl, amyl or hexyl)-glutarimide. This work is extended by determining the analeptic potency of bemegride as shown by its ability to reduce the sleeping time of mice given a prior dose of a hypnotic bearing a structural resemblance to the barbiturate ring system. It was found that bemegride significantly reduced the hypnotic activity of glutethimide, Persedon (3:3-diethyl-2:4-diketo-1:2:3:4-tetrahydropyridine), Nodular (3:3-diethyl-5-methyl-2:4-diketopiperidine) and Dolitrone (5-ethyl-6-phenyl-2:4-diketometathiazane). M. M.

***p*-Biphenylmethyl-(($\pm$)-tropyl-α-tropinium) Bromide, Pharmacology of.** L. Gyermek and K. Nádor. (*Arch. int. pharmacodyn.*, 1957, **113**, 1.) The pharmacology of a new antiacetylcholine compound, Gastropin, is described. It is found to possess moderate antiacetylcholine effects on the isolated guinea pig ileum, rat uterus and frog heart. In the anaesthetised cat or dog it causes a transient fall in blood pressure, inhibits bladder contractions, decreases gastro-intestinal motility and salivary flow, counteracts the vagal slowing of the heart and blocks the superior cervical ganglion. In guinea pigs it is a potent bronchodilator agent. It also possesses a moderate mydriatic action and weak neuromuscular blocking activity. The toxicity of Gastropin lies in about the same range as that of atropine methyl bromide. Thus it may be seen that this substance, as well as possessing moderate anticholinergic activity, also possesses ganglion blocking action. On the basis of these pharmacological results Gastropin is now being tested clinically. M. M.

Chlorothiazide, Electrolyte Excretion as Influenced by. K. H. Beyer Jr., J. E. Baer, H. F. Russo and R. Noll. (*Science*, 1958, **127**, 146.) Chlorothiazide (6-chloro-7-sulfamyl-1:2:4-benzothiadiazine-1:1-dioxide) induces changes in electrolyte excretion similar to those caused by organomercurial diuretics. Under reasonably normal conditions of acid-base balance, the effect of chlorothiazide is to increase the excretion of sodium, chloride and water. The excretion of potassium and bicarbonate is increased slightly, if at all. The effect of this drug on the ratio of sodium to chloride excreted per unit time varies

according to the state of electrolyte balance. This chloruresis distinguishes it from the carbonic anhydrase inhibitors that cause a predominant increase in bicarbonate rather than in chloride excretion. Chlorothiazide is also capable of counteracting the sodium and fluid retention induced by steroids such as 9α-fluorohydrocortisone. M. M.

Glucose Nitrates, Vasodilator Action of. D. O'Meara, D. M. Shepherd and G. B. West. (*Arch. int. pharmacodyn.*, 1958, **113**, 432.) Relatively little evidence is available as to the factors which may be of importance in determining the extent and duration of the vasodilator action of organic nitrates. A series of glucose derivatives, some partially nitrated, others fully nitrated, were examined to determine the relationship between their molecular structures and their pharmacological actions. Methyl β-D-glucoside was chosen as the parent compound, since its ring structure and stereochemical configuration are fixed and its nitrates are readily obtained in the pure crystalline form. The vasodilator activity was assessed by measuring the extent and duration of the fall in blood pressure of a dog after intravenous injection of 1 mg./kg. of each nitrate and comparing the response with that of erythritol tetranitrate. It was found that compounds containing one or two nitrate groups per molecule were inactive, but those containing three or four nitrate groups possessed depressor activity comparable with that of erythritol tetranitrate. In no case were the depressor effects diminished by prior administration of atropine and/or mepyramine. On oral administration to dogs, methyl β-D-glucoside tetranitrate produced a greater and more prolonged fall in blood pressure than did erythritol tetranitrate. No correlation was found between the depressor activity and the amount of nitrite ion released by the nitrates on alkaline hydrolysis. M. M.

Methylpentynol Carbamate. A. H. Galley and P. Trotter. (*Lancet*, 1958, **1**, 343.) Methylpentynol carbamate was given as premedication for dental operations under local anaesthesia to over 10,000 ambulant outpatients in the following dosage: Patients without visible signs of apprehension, two 100 mg. tablets; mildly apprehensive patients, four 100 mg. tablets; very apprehensive patients, 100 mg. per stone bodyweight. Of the 10,000 patients so treated 90 per cent showed no apprehension during operation, 7 per cent were apprehensive, and 3 per cent were very apprehensive. Methylpentynol carbamate took longer to act than methylpentynol, but the effect lasted longer. It was also shown to possess advantages over pentobarbitone for premedication in ambulant patients before dental extractions under general anaesthesia. The best results were obtained when it was reinforced with hyoscine sublingually in a dose of 1/150 gr. to children up to 12 years of age, and 1/75 gr. to those over this age. Used with either hyoscine or atropine, it was also found preferable to pentobarbitone as premedication before general surgical operations under general anaesthesia. After barbiturates, withdrawal or struggling is the usual reaction to an intravenous injection, but after methylpentynol carbamate this rarely occurs. Either the drug is to some extent analgesic or it provides a central nervous sedation, in contrast to the increased nervous excitability produced by the barbiturates. In contrast to the barbiturates, laryngeal spasm does not occur after giving methylpentynol carbamate. It therefore provides a much easier change-over to ether after induction with nitrous oxide and oxygen and laryngospasm is rare during throat operations where light anaesthesia is maintained and an endotracheal tube is not used. It does not cause respiratory depression, and has a low toxicity and no undesirable side-effects. S. L. W.