ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Adrenaline and Noradrenaline, Effect of Light on Fluorescence of Ethylenediamine Derivatives of. A. Goldfien and R. Karler. (*Science*, 1958, **127**, 1292.) After incubating a mixture of adrenaline and noradrenaline with ethylenediamine the fluorescence of the two compounds differs so that at 500 mμ the ratio of fluorescence of adrenaline to noradrenaline is 0·98 and at 550 mμ it is 4·4. This report shows that entirely different ratios can be obtained when the procedure is carried out in a room illuminated by light of different wavelengths. About 80 per cent of the fluorescence due to noradrenaline was lost if the procedure was carried out in daylight. Duplicate solutions of adrenaline and noradrenaline were prepared and samples were read at intervals of 5 mμ on the spectrophotofluorimeter, one procedure being carried out in a room illuminated by a 25-watt ruby lamp. Daylight, in addition to causing a loss of fluorescence of noradrenaline, also caused a small shift in the fluorescence maxima. Little effect was noted on the fluorescence of adrenaline. W. C. B.

Analgesics of the Morphine Group, Identification of. H. Baggesgaard Rasmussen, J. Berger, K. Folting and G. Espersen. (*Dansk Tidsskr. Farm.*, 1958, **32**, 81.) The picrates of morphine, codeine, ethylmorphine, nalorphine, dihydromorphinone, dihydrocodeinone and dihydrohydroxycodeinone were prepared, but they proved to be unsuitable for identification purposes as their melting ranges extended over an interval of 10–20°. A further difficulty was that some of the picrates contained water of crystallisation which could not be removed by drying over silica gel. Acetyl derivatives were found to be satisfactory for identification purposes. They were prepared by refluxing the morphine derivatives with acetic anhydride and sodium acetate, and isolated by pouring the reaction mixture into water and neutralising with sodium carbonate. The derivatives were purified by recrystallisation from ethanol, and gave reproducible melting points which are tabulated below. The bases may be recovered by precipitation with ammonium hydroxide solution, and, except in the case of morphine, the melting point provides an additional check on the identity of the compound.

Base	Melting point °C.	Melting point of acetyl derivative °C.
Morphine	—	173
Codeine	155–158·5	133·5
Ethylmorphine	87–90	130–131
Nalorphine	208–209	137·5–138·5
Dihydromorphinone	263–268	162·5–163
Dihydrocodeinone	197–200	154–155
Dihydrohydroxycodeinone	220–225	(1) 208 (2) 214

(1) = Diacetyl derivative. (2) = Monoacetyl derivative.

G. B.

Sulphonamides, Identification of, by Fluorescent Microscopy. I. Tschudi-Steiner. (*Pharm. Acta Helvet.*, 1958, **33**, 105.) This method depends upon the crystalline form and fluorescence when observed under a fluorescence microscope of Schiff's bases formed *in situ* on the microscope slide from sulphonamides with free primary aromatic amino groups and various aromatic aldehydes. The sulphonamides chosen were sulphadiazine, sulphamerazine, sulphadimidine and sulphasomidine and the aldehydes were *p*-dimethylaminobenzaldehyde, *p*-hydroxybenzaldehyde, salicylaldehyde, anisaldehyde, cinnamaldehyde and piperonal. These aldehydes gave fluorescent Schiff's bases with at least one of the four sulphonamides. The crystalline forms were also characteristic.

D. B. C.

Vitamin A, a New Spectrophotometric Method for the Assay of. I. M. Jakovljevic, (*Pharm. Weekbl.*, 1958, **93**, 585.) This depends upon the formation of a red colour with phosphotungstic acid in a chloroformic solution of the vitamin in the presence of a certain amount of acetic anhydride. 50 to 300 I.U. gives a suitable colour intensity. Cod-live oils and vitamin A concentrates are saponified with N alcoholic caustic potash solution, extracted with benzene, and an aliquot part of the dried benzene solution is evaporated in a stream of carbon dioxide below 40° and the residue dissolved in chloroform before the reagents are added. The colour formed is blue at first but changes to red and the mixture is allowed to remain in darkness for one hour for the colour to become stable, absorption maximum 538–540 mμ. The effect of varying the concentration of the reagents and the time and temperature of the reaction is examined.

D. B. C.

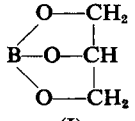
ESSENTIAL OILS

Mint Oils, Some New Constituents of. R. H. Reitsema. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 265.) Dihydrocarvone was shown to be present in some oils of the spearmint type. Its presence in oil from *Mentha niliaca* was demonstrated by reaction with 2:4-dinitrophenylhydrazine in ethanol, to form the dinitrophenylhydrazone. Similarly, dihydrocarvone was detected in oil from *M. crispa*, after removal of carvone. Jasmone was shown to be present in this oil after removal of carvone and alcohols. The oil from *M. aquatica* was found to contain about 40 per cent of menthofuran, determined by infra-red absorption at 733 cm.$^{-1}$, and pure menthofuran was isolated from the oil in a yield of 34 per cent. The oil of *M. sylvestris*, which had previously been reported to contain piperitone oxide, was found to contain the related compound diosphenol, a substance which is present in buchu leaves. By means of fractional distillation and chromatography it was shown that the oil also contains diosphenolene, piperitone, piperitenone, limonene and cineole. G. B.

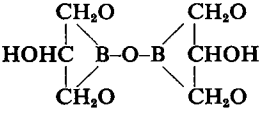
ORGANIC CHEMISTRY

Glyceryl Borate, Constitution of. W. Gerrard and E. F. Mooney. (*Chem. Ind.*, 1958, 227.) The authors have studied the formula for glyceryl borate put forward by Ahmad and Khundkar (I) and failed to prepare a structure corresponding to this formula, which shows a remarkable distortion of valency angles and which could not be constructed satisfactorily with Fischer-Herschelder models. It was considered that the difficulty would be overcome by the formation of a B–O–B structure. The product from boron acetate and glycerol was

a white amorphous powder which, contrary to Ahmad and Khundkar, could not be crystallised from acetone and was not soluble in ethyl acetate. The boron/glycerol ratio was closely 1:1 (found, B, 9·8 per cent) and the molecular weight determined ebullioscopically was 216. The infra-red spectra showed the presence of OH groups and of the B–O–B structure present in the tetra-acetyl diborate. With thionyl chloride, behaviour indicated the presence of a hydroxyl group, and the weight of water evolved after the formation of the polymer of high molecular weight corresponded to one hydroxyl group for each atom of boron. The structure II is suggested for glyceryl borate.



(I)



(II)

J. R. F.

Morphine, "Bound", Studies on the Structure of. J. M. Fujimoto and E. L. Way. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 273.) "Bound" morphine obtained from the urine of human addicts was shown, as follows, to be identical with a morphine conjugate from dog urine. After hydrolysis, a dinitrophenol derivative was prepared which gave an X-ray diffraction pattern identical with that of morphine dinitrophenyl ether. The identity of the glucuronic acid moiety was confirmed by examination of the infra-red spectrum and by the colour reaction with naphthoresorcinol and carbazole. Quantitative analysis indicated that the conjugates from human and dog urine were morphine glucuronates of identical composition. From an examination of the infra-red absorption spectrum and the pK values calculated from the two points of inflection of the titration curve it is postulated that at pH 5·8 the substance exists almost entirely in the form of a zwitterion. G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Glycyrrhetinic Acid Inhibition of Metabolism of Steroids *In Vitro*. L. M. Atherden. (*Biochem. J.*, 1958, **69**, 75.) This paper may explain the effectiveness of glycyrrhetinic acid in dermatological conditions. It has been shown that glycyrrhetinic acid is *in vitro* a powerful inhibitor of the metabolism of both 11-deoxycorticosterone and progesterone by rat-liver homogenates, both in the absence and in the presence of added reduced diphosphopyridine nucleotide. With rat liver particle free supernatant the metabolism of progesterone was completely inhibited by 0·0001M glycyrrhetinic acid in the presence of triphosphopyridine nucleotide and in the absence of *iso*citrate. Evidence that the active moiety of glycyrrhetinic acid is the $\alpha\beta$-unsaturated ketone group was provided by the observation that metabolism of progesterone is unaffected by 0·005M 11-deoxyglycyrrhetinic acid, methyl vinyl ketone or *p*-benzoquinone. The 11-oxo group is required for the inhibition. This may explain why Groen and others found glycyrrhetinic acid to have a 11-deoxycorticosterone sparing effect in Addison's disease and that analogues of glycyrrhetinic acid without the 11-oxo group were ineffective. G. F. S.

Penicillin, Chloramphenicol and Tetracycline, Penetration of Human Red Cells by. K. C. Watson. (*J. Lab. clin. Med.*, 1958, **51**, 778.) Solutions of the antibiotics were added to packed human red cells and the mixtures were then incubated. After incubation the tubes were centrifuged and the supernatant was removed. The cells were then washed with sterile saline before being haemolised with distilled water and repeated freeze-thawing. Finally the disrupted cell suspensions were assayed for antibiotic content. Penicillin appeared to be able to penetrate the cell wall to approximately 10 per cent of the extracellular concentration. Similar results were obtained whether the penicillin solution was made in saline or in plasma showing that penetration is independent of any plasma factor. Tetracycline appeared to pass into the red cell to a greater extent than penicillin but chloramphenicol was found to be unable to pass the cell wall barrier in active form in the concentrations used. In a further series of experiments with penicillin the haemolised blood, obtained by the above-mentioned procedure, was centrifuged and the supernatant haemoglobin solution removed. Assays carried out on both the haemoglobin solution and the deposited cell membranes showed that the antibiotic was contained only in the haemoglobin solution. W. C. B.

BIOCHEMICAL ANALYSIS

Antibiotics, A Modified Method for Evaluation of Clinical Usefulness of. I. Hoette and A. P. Struyk. (*J. Lab. clin. Med.*, 1958, **51**, 638.) A modified paper disc agar diffusion method is described for determining the sensitivity, to various antibiotics, of micro-organisms associated with infections. The method is designed so that the concentration of antibiotic at a zone diameter of 10 mm. is equivalent to that which can easily be obtained clinically as blood or urine level by the usual antibiotic therapy. Zone sizes greater than 10 mm. therefore indicate the suitability of the antibiotic for clinical treatment of the patient. The preparation of a special disc for differentiating between penicillinase and non-penicillinase staphylococci is described. Comparative experiments indicated that a good correlation exists between results obtained with the modified paper disc method and those obtained with the dilution method.
W. C. B.

Urinary Catechol Amines, Determination of. R. B. Johnson. (*J. Lab. clin. Med.*, 1958, **51**, 956.) A method is described for the estimation of urinary adrenaline and noradrenaline which incorporates a rapid chromatographic column isolation with a fluorimetric analysis, so giving an increased specificity. Collect 24-hour specimens of urine in bottles containing 10 ml. of 6N hydrochloric acid and 2 g. of oxalic acid crystals and store in a refrigerator. Measure the volume, adjust to 1500 ml. with distilled water, filter and collect 150 ml. of filtrate. Adjust to pH 1·5 with 6N hydrochloric acid and divide into three 50 ml. aliquots. One of these is used to determine recovery following the addition of 10 μg. of noradrenaline. Heat the aliquots in a boiling water bath for 15 minutes, cool and add 30 ml. of acetate buffer (pH 8·5) and adjust to pH 8·5 by slow addition of 25 per cent sodium carbonate solution. Pour immediately onto alumina columns (prepared by adding 5 ml. of 0·2M sodium acetate solution to 2·5 g. of alumina and washing into chromatographic columns 14 mm. by 30 cm.), and allow to pass rapidly. Wash the alumina with 10 ml. of acetate buffer and then with 50 ml. of distilled water. Add 0·25N sulphuric acid and allow the eluate to pass at a decreased speed. When acid to bromothymol blue collect 10 ml. and analyse this stable eluate for fluorescent substances as follows. Place 0·2 ml. (0·2 μg.) of working standards of adrenaline

and noradrenaline and 0·2 ml. of each eluate into a series of 15 ml. glass stoppered graduated tubes. Treat one tube of each as the blank adding 1 ml. of acetate buffer and 0·1 ml. of 0·25 per cent potassium ferricyanide. After exactly 2 minutes add 0·9 ml. of 20 per cent sodium hydroxide, mix and stand for 10 minutes. Do the same with the sample tubes but after the ferricyanide treatment add 1 ml. of a freshly prepared sodium ascorbate solution (9 parts of 5N sodium hydroxide and 1 part of 2 per cent ascorbic acid prepared 1 to 2 minutes before). 0·1 ml. of 2 per cent ascorbic acid is now added to the blanks and the timer set for 10 minutes. Add distilled water to 10 ml., mix and transfer aliquots to respective cuvettes. Compare the fluorescence in a photofluorimeter at the 10-minute period. Take three series of readings using primary filters at 365, 400 and 436 mμ and a secondary passing a narrow band at 510 mμ to measure emitted light. The adrenaline standard is set in all cases to read 50 and its blank zero. All other blanks and sample tubes are compared with this. For the calculation $\frac{\text{(Eluate sample minus eluate blank)}}{\text{(Nad. sample minus Nad. blank)}} \times 20 =$ μg. per cent total catechol amines as noradrenaline.

These values are determined for each wavelength. The method has a reproducibility of approximately ±10 per cent. G. F. S.

PHARMACY

Gum Tragacanth Jellies, Conditions for the Preservation of. A. Taub, W. A. Meer and L. W. Clausen. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 235.) Experiments were carried out with jellies containing 2 per cent of tragacanth and 5 per cent of propylene glycol, which was used to wet the gum. Jellies ranging from pH 3 to pH 7 were prepared by the addition of McIlvaine's buffer solutions. Four test organisms were used to assess the suitability of added preservatives, the jellies being inoculated and samples removed at intervals for plating. To obtain consistent results it was necessary to sterilise the jellies before inoculating with the test organism, *Micrococcus pyogenes* var. *aureus*, *Bacillus subtilis*, *Escherichia coli* or *Candida albicans*. Benzoic acid (0·2 per cent) was ineffective as a preservative at pH 7, but satisfactory at pH 5 and below. Chlorbutol (0·5 per cent) was satisfactory at pH 5, but not sufficiently active to prevent the growth of *C. albicans* at pH 7, and the activity against this organism decreased on continued storage. Methyl hydroxybenzoate (0·2 per cent) with propyl hydroxybenzoate (0·05 per cent) was satisfactory at pH 7 and below. G. B.

PHARMACOLOGY AND THERAPEUTICS

Anti-inflammatory Activity of Compounds Obtained from Egg-yolk, Peanut Oil and Soybean Lecithin. O. H. Ganley, O. E. Graessle and H. J. Robinson. (*J. Lab. clin. Med.*, 1958, **51**, 709.) Various fractions of peanut oil, soybean lecithin and egg-yolk were tested for anti-inflammatory activity in three different anti-inflammatory assays. Crystalline fractions of all three substances in a dose of 3 μg./kg. i.p. were effective in inhibiting the swelling of joints produced in the guinea pig by a local joint anaphylaxis reaction. The active factor in all cases was identified as *N*(2-hydroxyethyl)-palmitamide and the synthetic compound was found to be as active as the natural crystalline

product. Ethanolamine, a degradation product of *N*(2-hydroxyethyl)-palmitamide was also found to be active while palmitic acid was inactive. By substituting various groupings of ethanolamine, pharmacological activity was shown to be associated with a high degree of chemical specificity. The fractions were inactive both in the pellet assay in which an inflammatory response is produced in rats by implanting cotton pellets impregnated with a non-virulent culture of *Micrococcus pyogenes* var. *aureus* and in the Evan's blue test in rats in which inflammation, produced by the subcutaneous implantation of cotton pellets, is reflected by an increased permeability of the capillaries to the dye. W. C. B.

Dextromoramide (R875), Analgesic Activity of, in Student Volunteers. D. A. Cahal. (*Brit. J. Pharmacol.*, 1958, **13**, 30.) This compound, (+)-1-(3-methyl-4-morpholino-2:2-diphenylbutyryl)pyrrolidine, related to methadone, was found by Janssen to be a very potent analgesic in animal experiments. When injected into student volunteers it raised the threshold to ischaemic pain, the peak of analgesic activity being reached in two hours. Side effects were very marked even on the low dose (2·96 mg.), nausea and vomiting being very prevalent. Euphoria was absent, which is unusual in such a potent analgesic drug. There was evidence of an effect on voluntary muscle, many subjects experiencing muscular weakness, thirty minutes after the injection and hiccups and twitching two or three hours afterwards. Therapeutically the dose is limited by the severity of the side effects and should probably not exceed 6·0 mg. G. F. S.

Drugs, Absorption of, From The Rat Small Intestine. L. S. Schanker, D. J. Tocco, B. B. Brodie and C. A. M. Hogben. (*J. Pharmacol.*, 1958, **123**, 81.) The relative rates of absorption of a large number of drugs were measured by perfusing solutions of them through the entire length of the small intestine of the anaesthetised rat. The rate of absorption of those which were rapidly absorbed could be studied after a single perfusion of the small intestine. Others which were slowly absorbed were studied after continuous perfusion for 3 hours. No evidence for the existence of specific transport mechanisms was obtained indicating that absorption of drugs is a passive physical process. A relationship between the dissociation constant and the degree of absorption of compounds of widely different chemical structures was observed. Acidic drugs were rapidly absorbed if their pKa's were greater than 3. Basic drugs were rapidly absorbed if their pKa's were less that 8. The stronger acids and bases were relatively slowly absorbed and the absorption of very strong acids and bases was imperceptible. The authors conclude that absorption from the rat intestine can best be explained by assuming simple diffusion of unionised drug across a barrier which may be lipoid in nature. W. C. B.

Hypoglycin-A, an Hypoglycaemic Substance, Action of. P. C. Feng and S. J. Patrick. (*Brit. J. Pharmacol.*, 1958, **13**, 125.) The pharmacological and biochemical effects of hypoglycin-A were studied in animals. Hypoglycin-A is a substance isolated from the fruit of *Blighia sapida*, a tree growing commonly in the West Indies. Administration of lethal doses to kittens, guinea pigs and white rats initially caused drowsiness, lachrimation and secretion from the nose and mouth; vomiting was frequently observed in kittens. Autopsies performed immediately after death showed few gross pathological changes but suitable staining of histological sections showed a marked reduction in glycogen granules in the liver and a reduction of the granules of the alpha cells of the islets in the pancreas. Studies on the acute toxicity showed that previous fasting rendered rats much more susceptible to the toxic action of the compound. The most outstanding biochemical change produced by hypoglycin-A was a

pronounced hypoglaecemia which was preceded by exhaustion of liver glycogen. There were also smaller decreases in the glycogen stores of the heart, skeletal muscle and kidney without any increase in blood lactate or pyruvate. Hypoglycin-A lessened the effect of adrenaline on blood glucose and decreased both glucose tolerance and insulin sensitivity. It also decreased the oxygen consumption and carbon dioxide production of the intact rat. These effects are consistent with the hypothesis that the primary action of hypoglycin-A is the interference with glycogen production by the liver. Hypoglycaemia and low liver glycogen concentrations are found in patients suffering from "vomiting sickness". Evidence is therefore provided in support of the theory that the ingestion of the fruit of *Blighia sapida* is a cause of the disease in man.

W. C. B.

Noradrenaline, Relative Lack of Pharmacological Action of 3-Methoxy Analogue of. E. V. Evarts, L. Gillespie, T. C. Fleming and A. Sjoerdsma. (*Proc. Soc. exp. Biol., N.Y.*, 1958, **98**, 74.) The effects of 3-methoxynoradrenaline, an intermediate product in the metabolism of noradrenaline, were studied in the cat, the dog and in man. In cats under pentobarbitone anaesthesia, 3-methoxynoradrenaline in doses up to 2 mg. injected into the carotid artery was without effect on the transcallosal response. In unanaesthetised cats intravenous doses up to 10 mg./kg. were without effect on spontaneous cortical activity, recruiting responses, or the primary cortical responses to retinal photic stimulation or electrical stimulation of the lateral geniculate radiations. In a single study in the dog, 3-methoxynoradrenaline was shown to have only 1/500th or less of the pressor activity of noradrenaline. In two human subjects, the intravenous infusion of 3-methoxynoradrenaline in doses up to 5 mg. in 5 minutes did not produce any cardiovascular reactions nor were any psychological reactions observed. These findings suggest that *O*-methylation of noradrenaline *in vivo* results in its inactivation. W. C. B.

Nystatin Aerosol in Pulmonary Moniliasis. G. D. W. McKendrick and J. M. Medlock. (*Lancet*, 1958, **1**, 621.) A girl of 9 with fulminating influenzal pneumonia was given intramuscular penicillin and streptomycin, together with sulphadiazine by mouth. This prevented secondary staphylococcal infection. Bacteria, however, were superseded by *Candida albicans* and the extensive moniliasis which developed might well have proved fatal. As soon as *C. albicans* was seen in the sputum treatment with nystatin was started; 500,000 units was given 6-hourly by mouth for 8 days and 500,000 units 4-hourly by nebulizer into the oxygen tent for 4 days. The solution was made by mixing 500,000 units of Mycostatin with 15 ml. of distilled water to a fine suspension and atomising this at a flow of 6 litres a minute. The *C. albicans* quickly disappeared from the sputum and the patient's general condition began to improve from the first day of treatment and continued until she was eventually discharged 5 weeks after admission. It is thought that the inhalations were the decisive factor in recovery as nystatin is poorly absorbed from the intestinal tract.

S. L. W.

Pteroylglutamic Acid, Effect of, on the Serum Vitamin B_{12} Concentrations in Pernicious Anemia in Relapse. J. Bok, J. G. Faber, J. A. de Vries, W. F. Stenfert Kroese and H. O. Nieweg. (*J. Lab. clin. Med.*, 1958, **51**, 667.) After determining the vitamin B_{12} level in the serum of 13 patients with pernicious anaemia in relapse, pteroylglutamic acid (PGA) was administered orally in doses of 15 mg. per day for varying periods ranging from 4 to 8 days. The serum vitamin B_{12} level was again estimated on the last day of treatment. In 10

out of 11 cases which showed a haemopoietic response, a decrease of the serum vitamin B_{12} activity was demonstrated. In the remaining 2 cases, treatment with PGA did not increase blood formation and the serum vitamin B_{12} level showed no change. A correlation was established between the decrease in serum vitamin B_{12} level and the haemopoietic activity of PGA. W. C. B.

Pempidine (1:2:2:6:6-Pentamethylpiperidine). A New Hypotensive Drug. G. E. Lee, W. R. Wragg, S. J. Corne, N. D. Edge and H. W. Reading. (*Nature, Lond.*, 1958, **181**, 1717.) The preparation of 1:2:2:6:6-pentamethylpiperidine (pempidine) is described. This compound, which has been independently and contemporaneously developed and studied in another laboratory (see Spinks and Young, *Nature, Lond.*, 1958, **181**, 1397), was shown to possess about 1·4 times the activity and about eight times the duration of action of hexamethonium in causing relaxation of the preganglionically stimulated nictitating membrane of the anaesthetised cat. Further experiments, carried out on the anaesthetised cat and the isolated ileum of the guinea pig, localised the site of action of the drug at the autonomic ganglia. There was no evidence that large doses caused the release of histamine and neuromuscular block was produced only by very large doses. The *in vitro* anti-acetylcholinesterase action was shown to be negligible. Large doses of the compound were required to decrease the rate and amplitude of the contractions of the Langendorff rabbit heart. No adverse effects were observed on the blood picture of guinea pigs injected daily with the compound for 4 weeks and very large doses were required to cause a 50 per cent reduction in the growth rate of young rats. The compound was rapidly and well absorbed on oral administration. The pharmacological properties of pempidine appear to resemble those of the secondary amine, mecamylamine but it possesses potential advantages over mecamylamine in respect of tolerance, duration of action and excretion. W. C. B.

Pernicious Anaemia, Oral Treatment of. J. G. Heathcote and F. S. Mooney. (*Lancet*, 1958, **1**, 982.) The ineffectiveness of vitamin B_{12} by mouth in pernicious anaemia has been ascribed to the absence of an "intrinsic factor" in the gastric juice, necessary for its absorption. When given with normal gastric juice it is active in very small doses. The intrinsic factor has never been isolated and Heathcote and Mooney doubt its existence. They believe that the fundamental cause of pernicious anaemia is an inability to absorb vitamin B_{12}, due to the failure of simple proteolysis in the stomach through the absence of the secretion of gastric juice. For absorption the vitamin must be in the form of a simple peptide complex of low molecular weight, dialysable and assimilable by micro-organisms. Thus combined B_{12} in the food must first be digested, and pure crystalline B_{12} combined with a peptide before absorption in the intestine can occur. An active vitamin B_{12} peptide complex (H.P.P.) was prepared from a fermentation of Streptomyces, dialysable and ultra filtrable through Cellophane and collodion membranes. The preparation has been shown clinically to be the most effective oral preparation yet described. Six newly diagnosed cases of pernicious anaemia, treated exclusively with this oral preparation, showed a good haematological and clinical response which has been maintained from 140 to 290 days. A reticulocyte crisis consistently developed at the end of the first week and no case developed signs of cord deterioration. A seventh case showed early subacute combined degeneration of the cord, following treatment with another oral preparation. Oral treatment with HPP ameliorated the symptoms and an unequivocal subjective improvement took place. G. F. S.

Perphenazine in Post-operative Vomiting. C. F. Scurr and D. S. Robbie. (*Brit. med. J.*, 1958, **1**, 922.) The efficacy of perphenazine (1-(2-hydroxyethyl)-4-[3-(2-chloro-10-phenothiazinyl)-propyl]-piperazine in post-operative vomiting was investigated in 200 consecutive patients undergoing various operative procedures. Alternate patients received perphenazine 5 mg. by intramuscular injection in the right thigh at the end of operation, the remainder serving as controls. The vomiting rate was 21 per cent in the controls and 7 per cent in those receiving perphenazine. The mean recovery time was 17 minutes in the controls and 27 minutes in the perphenazine series. More females vomited than males, in the ratio of 2·5 : 1. There was no indication that any differences between the two groups regarding pre-medication, anaesthetic agent, or operation contributed significantly to the difference in vomiting rate. No side-effects of the drug were observed. The drug has some potentiating effect on barbiturates and other narcotics, but the effect is much less than with chlorpromazine. The main danger is that perhaps, like chlorpromazine, the drug can obscure the cause of vomiting due to organic disease. S. L. W.

Serotonin Antagonism, Comparative Study on, of Amide Derivatives of Lysergic Acid and of Ergot Alkaloids. A. Cerletti and W. Doepfner. (*J. Pharmacol.*, 1958, **122**, 124.) The antiserotonin activity of more than forty ergot derivatives and about thirty semi-synthetic derivatives of lysergic acid has been determined on the isolated rat uterus. The degree of specificity was assessed by determining simultaneously the acetylcholine antagonism of the different compounds. Doses of serotonin were given at 10 minute intervals and the antagonist applied once only during the interval. With the amide derivatives none reached the activity of (+)-lysergic acid diethylamide (LSD). The most active was the monoamylamide of lysergic acid. Three isomers of LSD and Lumi-LSD were practically ineffective. Dihydro-LSD maintained 50 per cent of the activity of the original product. With the natural and hydrogenated alkaloids of ergot, all the peptide alkaloids—ergotamine and ergotoxine derivatives—with the exception of dihydroergotamine, showed less than 10 per cent of the activity of LSD. The ergonovine group were quite active antagonists, the most active being the methyl derivative which had 61 per cent of the activity of LSD. Substances with antiserotonin activities higher than LSD were found within the group of LSD derivatives with different substitution on the ring structure of LSD. The most potent compound so far studied was 1-methyl-2-bromolysergic acid diethylamide. G. F. S.

Urocanoylcholine (Murexine), Pharmacological Properties of. M. J. Keyl and V. P. Whittaker. (*Brit. J. Pharmacol.*, 1958, **13**, 103.) Urocanoylcholine (2-β-imidazol-4(5)-ylacryloyloxyethyl) trimethylammonium bromide) is a naturally occurring choline ester first identified by Erspamer in three Mediterranean species of whelks. The compound has been found to have both ganglion stimulating and neuromuscular blocking actions. In the dog a small dose (50 μg./kg.) has a slight vasodepressor action and by increasing the dose to 500 μg./kg. this is followed by a vasopressor response antagonised by T.E.A. Neuromuscular blockade was due to depolarisation of the end plate region and as with decamethonium, cats were most sensitive and rats least sensitive. The action of urocanoylcholine was short-lasting in all species, but this was not due to hydrolysis by plasma esterases. G. F. S.