ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Acriflavine, Polarographic Determination of. A. J. Zimmer and K. Mansur. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 204.) Solutions of acriflavine were examined polarographically. It was established that although acriflavine is a mixture it behaves as a single compound the half-wave potential in acid solution *p*H 1·1, after the removal of oxygen, being given by the equation $E_{\frac{1}{2}} = 0{\cdot}39\ \text{V} + 4{\cdot}8\ c$ for the first wave and $E_{\frac{1}{2}} = 0{\cdot}59\ \text{V} + 4{\cdot}8\ c$ for the second wave, where c is the percentage concentration. The waves were well defined and independent of the supporting electrolyte. They were affected by changes in the hydrogen ion concentration, and in neutral or alkaline solutions the electrode reaction was irreversible for the first wave. The polarographic method of analysis was applied to preparations, including tablets and ointments and was more accurate and convenient than that of the U.S. National Formulary (9th edition), which also suffers from the disadvantage of determining only the chloride ion, and not the active acridine compounds. G. B.

Amanita Toxin, Chemical Identification of. S. S. Block, R. L. Stephens, A. Barreto and W. A. Murrill. (*Science*, 1955, **121**, 505.) The following procedure was used. Mince a sample of 0·1 g. or more of fresh fungus and extract by boiling in methanol. Filter or centrifuge the extract and evaporate the liquid to dryness on a water bath. Redissolve the residue in a little methanol and submit the solution to paper chromatography using methyl ethyl ketone, acetone, water and butanol (20:6:5:1) as the solvent. Spray the dried chromatogram with a 1 per cent. solution of cinnamaldehyde in methanol. Violet spots indicate the presence of amanitines and bright blue spots are due to phalloidine. This method was applied to 46 species, and only the poisonous ones gave a positive reaction for amanitines. An exception was observed in the case of *Lepiota cretacea* which gave a weak violet colour although it was not toxic. *Amanita muscaria*, which contains the quicker-acting poison muscarine, was not submitted to the test. G. B.

Barbiturates, Potentiometric Non-aqueous Assay for. C. J. Swartz and N. E. Foss. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 217.) When pure chloroform is used as a non-aqueous medium for the titration of barbiturates, the end-point cannot be determined accurately by potentiometry. This disadvantage may be overcome by the addition of polyethylene glycol 400, the sharpest end-point being obtained when chloroform containing 10 per cent. of polyethylene glycol 400 is used. The following is an accurate and convenient method of assay. Dissolve 0·1 to 0·2 g. of the dried barbituric acid under test in 5 ml. of polyethylene glycol 400 and 45 ml. of chloroform, and titrate with 0·1 N sodium methoxide in dehydrated methanol, the end-point being determined electrometrically. Sodium derivatives of barbituric acids should first be dissolved in water, the solution acidified, extracted with chloroform and the extract concentrated to 45 ml. After the addition of polyethylene glycol 400, the solution is titrated as above. G. B.

Magnesium Citrate Solution, Assay for. D. D. Abbott and L. A. Reber. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 287.) To a 10-ml. sample, freed from excessive carbon dioxide by repeated pouring, add sufficient water to produce 100 ml. To 25 ml. add 50 ml. of standard solution of sodium ethylenediaminetetra-acetate, allow to stand for 10 minutes, add 20 ml. of ammonium chloride/ammonium hydroxide buffer solution and titrate the excess of ethylenediaminetetra-acetate with standard solution of magnesium sulphate (1 mg. of Mg/ml.,) using "inhibited versenate" indicator solution, and titrating until the colour changes from dark blue to wine red. The standard solution of magnesium sulphate may be standardised by the hydroxyquinoline gravimetric method. The above method is rapid and comparable in accuracy with the U.S.P. XIV gravimetric method. For the determination of total citric acid, heat almost to boiling, 25 ml. of the diluted sample (see above) and pour it through a column of ion exchange resin (amberlite IR-120 (H)). Wash the sample through the column with 2 quantities each of 25 ml. of hot water, and titrate the effluent, containing the free acid, with 0·1N sodium hydroxide using phenolphthalein as indicator. This method, while not specific for citric acid, appears to give results comparable to those of the U.S.P. method of precipitation as calcium citrate, and the precision of the method is greater. G. B.

Opium, Determination of Morphine in. R. Fischer and K. Folberth. (*Arzneimitt.-Forsch.*, 1955, **5**, 66.) 1 g. of opium is rubbed down with 3 ml. of water, and the mixture is passed through a column of 10 g. of acid alumina (Woelm), being washed through with 5 ml. portions of water, using in all 35 ml. of water. The eluate is treated with 4 ml. of ammonia (23 per cent.), and made up to 40 g. with water. A solution of 0·25 g. of dinitrochlorbenzene in 30 ml. of acetone is then added, and the mixture is allowed to stand overnight in a cold place. The morphine ether is filtered off, washed with two 2 ml. portions of cold acetone, then with two 2 ml. portions of water, and dried for 2 hours at 70 to 80° C. The method may also be applied to tincture of opium, 10 ml. being evaporated to remove the ethanol and the residue taken up in 5 ml. of water. G. M.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Blood Cholinesterase Values in Excessive Exposure to Phosphorus Insecticides. J. C. Gage. (*Brit. med. J.*, 1955, **1**, 1370.) The red cell and plasma cholinesterase values of 19 normal subjects were measured at monthly intervals for 1 year. The coefficient of variation was 12·8 for red cell and 21·3 for plasma values, composed of a basic individual variation, increased by the experimental error of measurement and temporal variations of unknown origin. The following are suggested as criteria for the detection of excessive exposure to phosphorus insecticides. If an individual shows a red cell or plasma cholinesterase value less than ½ of the population average, or less than ½ of his pre-exposure value, whichever is the higher, he should not be allowed to continue his employment and measures to prevent excessive exposure of workers should be re-examined. A value between 50 and 60 per cent. of the population average indicates the need of special supervision with frequent determinations of the cholinesterase values of the workers involved. It is advisable to determine the normal cholinesterase value for each worker before he has been exposed to the insecticides, so that a more accurate assessment of the amount of anticholinesterase he absorbs can be made. G. B.

Kynurenine and 3-Hydroxykynurenine in Urine. L. Musajo, C. A. Benassi and A. Parpajola. (*Nature, Lond.*, 1955, **175**, 855.) Results are reported on the excretion of kynurenine and 3-hydroxykynurenine in pathological human urines. The urine of normal humans, used as control, gave negative results and the urine of several patients was also negative; in many others a slight excretion of metabolites was noted, mainly kynurenic and xanthurenic acids, anthranilic and 3-hydroxy-anthranilic acids and, sometimes, kynurenine and 3-hydroxy-kynurenine. A positive result was found in hæmoblastotic forms, 76 cases being examined. In 59, kynurenine and 3-hydroxykynurenine (both free and conjugated) were found in quantity with small quantities of kynurenic and xanthurenic acids; in 11 cases kynurenine was present, but 3-hydroxykynurenine was absent. In 6 subjects, some of uncertain diagnosis, the kynurenines were absent including 4 patients treated with a colchicin derivative which was considered to inhibit the excretion of the tryptophan metabolites. Excretion took place during both normal and fever periods; the recession of the fever did not stop the excretion. In 4 cases, quantities up to 40 mg. kynurenine sulphate and 16·4 mg. of 3-hydroxykynurenine were recovered from urine. R. E. S.

BIOCHEMICAL ANALYSIS

Adrenaline and Noradrenaline in a Mixture, Colorimetric Estimation of. T. Ozaki. (*Tohoku J. exp. Med.*, 1954, **61**, 83.) A method is described for the differential estimation of adrenaline and noradrenaline in a mixture. At *p*H 3·6 adrenaline is oxidised completely in 2 minutes with potassium permanganate while only 10 per cent. of noradrenaline is oxidised. At *p*H 5·6 both are completely oxidised within 3 minutes. For the estimation 0·1 to 1·0 ml. of the sample to be tested or a standard adrenaline solution is measured. The *p*H is adjusted to 3·6 or 5·6 by the addition of acetate-acetic acid buffer solutions, and 0·1 ml. of permanganate reagent added. (The permanganate reagent consists of 3 g. of potassium permanganate dissolved in 24 ml. of distilled water and 8 ml. of 75 per cent. lactic acid solution is added.) After 2 minutes at *p*H 3·6 or 3 minutes at *p*H 5·6, 0·05 per cent. hydrogen peroxide solution, in an amount equivalent to the permanganate, is added and the mixture is diluted with cold water to a volume of 6 to 10 ml. The oxidation with permanganate is always made at 20° C. The colour density of the test and standard are compared within 5 minutes in a colorimeter. The amount of adrenaline and noradrenaline is calculated from the formulas $A = X + n_{3\cdot6}.Y$ and $B = X + n_{5\cdot6}.Y$ where X and Y are the amount of adrenaline and noradrenaline respectively, A and B are μg. equivalents of adrenaline estimated at *p*H 3·6 and 5·6 respectively and $n_{3\cdot6}$ and $n_{5\cdot6}$ the colorimetric activity ratio of noradrenaline to adrenaline estimated at *p*H 3·6 and 5·6 respectively. The method has been used to assay the noradrenaline and adrenaline contents of the adrenals of cattle and horses. Noradrenaline was found in the medullary tissue in an amount of 29 per cent. of the total in cattle and 18·5 per cent. in the horse, which is in agreement with the findings of Holtz and Schuman and Shepherd and West. G. F. S.

Human Whole-blood Cholinesterase, Assay of. D. R. Davies and J. D. Nicholls. (*Brit. med. J.*, 1955, **1**, 1373.) Collect 20 cu. mm. of blood in a hæmoglobin pipette and wash it into 1 ml. of dilute solution of bromothymol blue in a test-tube. Add 0·5 ml. of a 0·6 per cent. solution of acetylcholine chloride in water, and observe the time required for the solution to become deep orange. The blood cholinesterase value may be read from a chart relating cholinesterase value to rate of change of *p*H during the test. A result 50 per cent. of the mean normal cholinesterase value (ΔpH/hour = 67) indicates that the level of

hypersensitivity to anticholinesterase has been reached, while 20 per cent. of the normal value (ΔpH/hour = 26) may be regarded as the clinical danger level. The lower fiducial limit of normal activity is 109 (ΔpH/hour). The above figures relate to determinations at 20° C. A chart is given showing the times corresponding to these limits, for determinations at 10 to 30° C. G. B.

Noradrenaline and Adrenaline in Urine, Chemical Determination of. A. Pekkarinen and M-E. Pitkänen. (*Scand. J. clin. Lab. Invest.*, 1955, **7**, 1.) The adrenaline and noradrenaline contained in the urine sample are adsorbed on to aluminium oxide at *p*H 8·5 and subsequently eluted with oxalic acid. Care is taken to eliminate all interfering substances. The solution is then treated with manganese dioxide and the fluorescence of the resulting adrenalutine or noradrenalutine is measured. The two substances are distinguishable by the difference in the time that they take to reach maximal intensity. About 70–80 per cent. recovery of either amine from the urine is obtained. M. M.

Steroids, Extraction of, from Blood. M. E. Lombardo, P. H. Mann, T. A. Viscelli and P. B. Hudson. (*J. biol. Chem.*, 1955, **212**, 345.) A simple method is described for the estimation of steroids in blood, combining dialysis and extraction in one operation. Equal volumes of blood, water and methanol are placed in Cellophane dialyzing tubing and extracted with 60 per cent. aqueous methylene chloride in a special extractor. The extracts are evaporated to dryness on a water bath at 40° C. *in vacuo* and then chromatographed in an appropriate solvent system. All steroids possessing a Δ^4-3-ketone group are located on the paper as ultra-violet-absorbing areas. Steroids such as androsterone and dehydroepiandrosterone are detected with the Zimmerman reagent. The steroid containing zones on the paper are cut into tiny squares and eluted quantitatively with a methanol-chloroform mixture. Steroids possessing the Δ^4-3-ketone group are estimated by their absorption at 238 to 242 mμ in a Beckman spectrophotometer. Compounds such as deoxycorticosterone, Compound E, Compound F can also be determined by the blue tetrazolium method, and except Compound E by the Porter-Silber reaction. The results of recovery experiments with various steroids at different concentrations are reported. The method is useful for the analysis of adrenal venous blood. G. F. S.

Xanthines and Organic Mercurials, Bioassay and Diuretic Potency of, in Humans. T. Greiner, H. Gold, F. Palumbo, L. Warshaw, T. McGowan, J. Weaver and H. Otto. (*J. Pharmacol.*, 1955, **113**, 140.) A method for the bioassay of diuretic substances, using ambulant patients with congestive heart failure, is described and the results analysed statistically. The diuretic effect is measured by the loss of body weight 24 hours after the dose. This method is used to compare the potency of aminophylline with meralluride (Mercuhydrin), to determine the degree to which the diuretic action of meralluride may be augmented by aminophylline, to compare the diuretic action of aminophylline by intramuscular and oral administration and to compare the therapeutic value of oral theophylline in the form of the ethylenediamine with that of the calcium salt. It was found that 0·5 g. of aminophylline causes a diuretic effect equal to that of 0·6 ml. of meralluride, both being given intramuscularly, but that aminophylline is less effective orally. In terms of molecular weight, aminophylline and calcium theophyllinate have equal diuretic potency. Aminophylline may enhance the diuretic activity of the organic mercurials by approximately 50 per cent. This is due to a simple summation of effects and not to a potentiation. There is, however, insufficient evidence that the xanthines will restore a diuretic response in patients refractory to the organic mercurials.

M. M.

CHEMOTHERAPY

Antibiotic of Bacterial Origin, A New. A. T. Fuller. (*Nature, Lond.*, 1955, **175**, 722.) This antibiotic was isolated from a spore-bearing organism of the *Bacillus pumilis* group, obtained from an East African soil. It was prepared in good yield by growing the organism in aerated culture in a medium containing inorganic salts, ammonium citrate, glucose and meat extract. The antibiotic was isolated by acidifying to *p*H 2·5, precipitating with ammonium sulphate, extracting the precipitate with ethanol, evaporating to dryness, washing the residue with ether to remove impurities, dissolving the remainder in ethanol and passing the solution through an alumina column. The eluate was recrystallised from a mixture of acetic acid and ethyl acetate, in the form of a white solid, melting point 252° C., empirical formula $C_8H_9O_2N_2S$. It was effective *in vitro* against *Streptococcus aureus, Pasteurella muriseptica, Streptococcus hæmolyticus* group A and *Mycobacterium tuberculosis.* It was not active against *Bacterium coli, Shigella flexnerii* or *Candida albicans.* Administered intraperitoneally to mice it was non-toxic and effective against hæmolytic streptococcal infections. It was less effective when given by mouth. G. B.

Ethylene Bis-dithiocarbamate Esters as Fungicides. A. P. Collins and G. A. Wiese. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 310.) Disodium ethylene bis-thiocarbamate was prepared by the reaction of a solution of ethylenediamine and sodium hydroxide with carbon disulphide. The resulting solution was used directly for the preparation of the bis-2-hydroxyethyl, bis-3-hydroxypropyl and di-*n*-propyl esters. The isolated salt, prepared by a modified procedure, was used for the preparation of the diallyl and dibenzyl esters. All these esters were tested for activity against pathogenic fungi (*M. audouini, A. schoenleinii, M. lanosum, M. gypseum* and *T. rubrum*) using paper discs impregnated with acetone solutions of the fungicides, which were placed on plates of medium streaked with the organism. Zones of inhibition were measured after incubation for 7 days at 37° C. The diallyl ester was more active than undecylenic acid against all the test organisms. Bis-2-hydroxyethyl, bis-3-hydroxypropyl and di-*n*-propyl esters were of about the same order of activity as undecylenic acid. A certain amount of specificity of action was observed, the bis-2-hydroxyethyl ester being much more active against *M. lanosum, M. gypseum* and *T. rubrum* than against the other organisms. G. B.

PHARMACY

NOTES AND FORMULÆ

Aspirin, Decomposition of, in Aspirin, Phenacetin and Caffeine Tablets. D. Ribeiro, D. Stevenson, J. Samyn, G. Milsovich and A. M. Mattocks. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 226.) Experimental batches of aspirin, phenacetin and caffeine tablets were prepared to determine the effect of varying the form of aspirin, lubricant, moisture content and pressure in the tablet machine. The tablets were stored at 45° C. for 4 weeks and the decomposition assessed in terms of the content of salicylic acid, determined by measuring the colour intensity after reaction with ferric ammonium sulphate. Stearic acid and stearates caused significantly greater decomposition than talc, mineral oil or Aldo 33, especially when a large proportion of lubricant was included. Crystalline aspirin was preferable to aspirin-starch granulation made by precompression, especially when Aldo 33, stearic acid, talc or mineral oil

were employed. A moderate water content of the phenacetin-caffeine granules did not increase the rate of decomposition, and variations in the pressure applied to the machine punches had no effect on the keeping properties of the tablets. G. B.

Neomycin in Pharmaceutical Preparations, Stability of. R. M. Simone and R. P. Popino. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 275.) Preparations were assayed before and after storage, using a cup-plate method, with *Bacillus subtilis* as the test organism. Aqueous solutions, tablets and soluble and water-miscible bases were diluted and assayed directly. Oily preparations were dissolved in ether/light petroleum mixture and extracted several times with phosphate buffer, *p*H 8, the mixed extracts being used for the test. Aqueous solutions appeared to be stable for up to 2 years at room temperature, the presence of 0·1 to 0·3 per cent. of antioxidant and buffering to *p*H 6 to 7 preventing the discoloration which otherwise occurs, especially in concentrated solutions (50 to 400 mg./ml). A series of nasal preparations, mouthwashes and tinctures were stable for 1 year at room temperature. Tablets, lozenges and ointments in water-miscible and water-immiscible bases were stable for 2 years, but a 4 per cent. ointment in hydrous lanolin lost 90 per cent. of its activity in 1 year at 23° C. Autoclaving of a 0·325 per cent. w/v solution of neomycin sulphate in water at 120° C. for 40 minutes caused no loss in potency. Preparations containing neomycin with penicillin, bacitracin or dihydrostreptomycin were equally stable. Sterilisation of dry powdered neomycin sulphate at 110° C. for 10 hours caused no loss in potency, but under similar conditions a 0·325 per cent. ointment in white petroleum jelly showed a loss of 13 per cent. with darkening of the preparation. G. B.

PHARMACOLOGY AND THERAPEUTICS

Acetazoleamide in Acute Respiratory Acidosis. M. Wishart and B. Isaacs. (*Lancet*, 1955, **218**, 995.) Acetazoleamide (Diamox) inhibits the enzyme carbonic anhydrase, its main pharmacological effect being exerted on the renal tubule cells, leading to increased urinary excretion of sodium, potassium, and bicarbonate; reduced excretion of ammonium ion; a rise in *p*H of the urine; and a fall in the serum bicarbonate level and in *p*H of the blood. Acetazoleamide was given to 3 patients with acute exacerbation of chronic respiratory acidosis in the hope of preventing or relieving carbon-dioxide narcosis. Increased urinary excretion of bicarbonate and a fall in the serum-bicarbonate resulted. In all 3 cases there was clinical deterioration—2 of the patients died and the third recovered when the acetazoleamide was withheld. It was concluded that in these 3 cases acetazoleamide was of no value, and that its property of promoting renal excretion of bicarbonate may have been harmful to the patients. S. L. W.

Adrenaline, Noradrenaline and Dihydroergotamine, Effects of, on Excised Human Myometrium. W. J. Garrett. (*Brit. J. Pharmacol.*, 1955, **10**, 39.) The action of (−)-adrenaline, (−)-noradrenaline and dihydroergotamine on isolated strips of human myometrium were investigated at various stages of the menstrual cycle, after the menopause, during pregnancy and at parturition. The myometrial segments from non-pregnant uteri were cut as vertical strips from the body of the uterus; those of pregnant uteri were transverse strips from the lower segment. Both adrenaline and noradrenaline stimulated the muscle under all the above conditions, noradrenaline being considerably the more potent on the non-pregnant uteri. The stimulant actions were blocked by dihydroergotamine and potentiated by cocaine. The *in vitro* results obtained

for adrenaline with the late-pregnancy strips differed from those obtained for this drug *in vivo*, where inhibition was the usual response. Noradrenaline stimulated the myometrium both *in vivo* and *in vitro*. G. P.

Anticholinesterase Agents, Effect of, on the Rats' Blood Pressure. P. Dirnhuber and H. Cullumbine. (*Brit. J. Pharmacol.*, 1955, **10**, 12.) Sarin, dyflos, eserine, TEPP and E600 all produced hypertension when administered to rats in near-lethal doses. Spinalisation of the rat, hexamethonium, tolazoline, ergotamine and large doses of atropine reduced the response to a small short-lasting rise in pressure. In the skinned rat the prolonged rise was also absent. It was concluded that the anticholinesterases increase, by a central action, the sympathetic tone in the blood vessels of the skin. G. P.

Antithyroid Drugs: Mode of Action, *In Vitro* Inhibition of Oxidative Protein Iodination. R. Fraser, M. G. W. Hanns and W. R. Pitney. (*Brit. J. Pharmacol.*, 1955, **10**, 1.) The mechanisms of action of antithyroid drugs were investigated by two *in vitro* tests. The first and more important test measured the inhibition by the drug of a protein-iodinating enzyme system, consisting of milk enzyme powder, xanthine, casein and radio-iodide. The other determined the interference with a non-enzymic casein iodination with peroxide and radio-iodine. In a series of known antithyroid drugs, differentiation of mode of action was possible from the results of the two tests. The first group (carbimazole, methimazole, 2-thiouracil and iodothiouracil) acted mainly by enzyme inhibition, the second group (resorcinol, sulphathiazole and isoniazid) had little enzyme-inhibiting activity and apparently acted mainly by iodine removal or by substrate competition, while the third group (thiocyanate, L-thyroxine and *p*-aminosalicylate) showed intermediate characteristics, but resembled more closely the second group. The enzyme test was suggested as a useful screening test for new antithyroid compounds since in the series tested the potency measured by this method correlated well with *in vivo* antithyroid activity. G. P.

Baytenal, A Short-acting Thiobarbiturate. P. Nobes. (*Lancet*, 1955, **268**, 797.) Baytenal is sodium 5:5-allyl-(2-methylpropyl)-thiobarbiturate, which is administered intravenously as a 10 per cent. aqueous solution as a very short-acting anæsthetic. Elimination is so rapid that there is virtually no post-operative somnolence. The drug was tried in 11 patients ranging in age from 17 to 62, selected so as to avoid the need for other intravenous medication. Some patients received Omnopon 1/3 grain and scopolamine 1/150 grain. Dosage of Baytenal was based on the age, weight and general condition of the patient and on the duration of the operation, and varied from 0·45 to 1 g. The drug was also given experimentally to a volunteer (the author). The most striking feature was the rapidity with which consciousness was regained and the freedom from post-anæsthetic confusion or drowsiness. The volunteer regained consciousness in 6 minutes and could write an account of his subjective sensations in 22 minutes. Slight euphoria persisted for 2 hours but did not interfere with work or ability to drive a car. In all cases respiratory depression was slight and apnœa was of short duration. Retching, lasting for ½ to 1 minute, occurred in only 3 cases, two of whom had been given Omnopon and scopolamine premedication. It is suggested that the drug may be especially useful for anæsthesia in out-patients or casualty cases. H. T. B.

B.C.G. Vaccination, Standardisation and Efficacy of, against Tuberculosis. S. R. Rosenthal. (*J. Amer. med. Ass.*, 1955, **157**, 801.) This is a critical evaluation of B.C.G. vaccination based on a 20-year study. With regard to

alleged loss in viability of B.C.G. vaccine, it has been shown that when standard vaccine is stored at ice-box temperatures it loses little of its viability for periods up to one month, and at these temperatures freeze-dried vaccine remains of constant viability for periods up to 3 years. With the freeze-dried vaccine it is now possible to completely standardise the vaccine before use; viability, potency and safety can all be ascertained before distribution. B.C.G. vaccine increases resistance against virulent tuberculosis in man in all age groups bringing about a reduction in the morbidity and mortality from tuberculosis of from 54 to 100 per cent. B.C.G. vaccination should be used only as a part of a tuberculosis control programme in which housing, nutrition and education are also taken into account. The multiple puncture method of vaccination is simple in application and devoid of complication, and leaves no scar. In this method a thin stainless steel disc with 36 sharp protrusions is used. A drop of vaccine is placed on the outer aspect of the arm over the deltoid region and is spread with the wide margin of the disc which is held by a stainless steel magnet. The skin is tensed from beneath with one hand and downward pressure is exerted on the magnet and disc with the other so that the needles puncture the skin through the vaccine. The vaccine is then redistributed with the wide margin of the disc into the apertures made by the disc. Small maculopapules appear after 10 to 14 days and disappear after a month or two. The rate of conversion is high (90 to 100 per cent.) and compares favourably with the results of other parenteral methods. S. L. W.

Cardiac Glycosides in the Treatment of Cardiogenic Shock. R. Gorlin and E. D. Robin. (*Brit. med. J.*, 1955, **1**, 937.) Hesitation about using cardiac glycosides in myocardial infarction is based on the facts that the experimentally infarcted heart shows lowered tolerance of digitalis and that the effects of digitalis and infarction, both of which increase the likelihood of ventricular irritability and arrhythmia, may be additive. The authors have used cardiac glycosides in 4 patients with myocardial infarction who were in both coma and shock. 1 patient in clinical shock was given lanatoside C and 3 with shock and pulmonary œdema were treated with ouabain, both drugs being given intravenously. All showed remarkable clinical response with a rise in blood pressure, decrease in pulmonary œdema and dramatic clearing of the coma. 3 out of the 4 ultimately survived. The first patient was given 50 mg. of procaine amide hydrochloride intravenously, with conversion to a normal sinus mechanism. Noradrenaline produced a rise in blood pressure but the clinical shock remained. 0·4 mg. of lanatoside C intravenously produced a marked response within 30 minutes; a further dose of 0·4 mg. was then given. Death occurred suddenly 1 hour later and post-mortem examination showed a fresh myocardial infarction and pulmonary congestion. Death may have been related to a digitalis induced arrhythmia. The ouabain treated patients were given respectively 0·15 mg. in 3 doses each of 0·05 mg., and single doses of 0·2 mg. and 0·125 mg. Supplementary treatment with morphine, oxygen, procaine amide hydrochloride and venesection was given when necessary. All came out of coma within 20 to 45 minutes and eventually made a complete recovery. The authors suggest the following treatment for myocardial infarction with shock—morphine for pain, adjustment of the patient's position in bed for its effect on blood pressure and venous return, phlebotomy for its effect on venous pressure, vasoconstrictor agents for increasing systemic resistance and arterial pressure, and cardiac glycosides for increasing cardiac output and arterial pressure. The importance of the dose of the cardiac glycosides in avoiding toxicity is emphasised. In this series 25 to 50 per cent. of the generally accepted dose of ouabain was found adequate. H. T. B.

Chlorpromazine, Action of, on the Autonomic Nervous System. F. Jourdan, P. Duchêne-Marullaz and P. Boissier. (*Arch. int. Pharmacodyn.*, 1955, **101**, 253.) The actions of chlorpromazine on autonomic pathways in the dog and the rabbit were studied, using in all cases the same dose, 5 mg./kg. intravenously, a dose which corresponds to that employed clinically. In the dog, blockade of adrenaline vasopressor effects was always obtained and reversal sometimes occurred. In the rabbit, however, only a moderate adrenergic blockade resulted, reversal never appearing. In the dog, chlorpromazine had no action on the cardioaccelerator action of adrenaline; on the contrary, the drug had an accelerator action of its own, which persisted after denervation of the heart. There was also no action on the mydriasis, exophthalmos, retraction of the nictitating membrane or conjunctival vasoconstriction resulting from stimulation of the cervical sympathetic trunk. Similarly, the cardioaccelerator effects of cervical sympathetic stimulation were not affected. Renal vasoconstriction following splanchnic nerve stimulation in the adrenalectomised dog was only moderately depressed. Release of adrenaline from the adrenal medulla on stimulation of the splanchnic nerve was not affected by chlorpromazine. Stimulation of the peripheral vagus was partly blocked, but the duration of action was prolonged, especially in the rabbit. Salivary secretory response to chorda stimulation was slightly decreased. The hypotensive and cardiac slowing effects of injected acetylcholine were not modified. In the dog, the hypotension induced by chlorpromazine was mainly central, no hypotension occurring in the spinal dog. Also, small doses, inactive when injected peripherally, led to a rapid fall in pressure when injected into the vertebral artery.

G. P.

Chlorpromazine, Psychiatric Use of. W. H. Trethowan and P. A. L. Scott. (*Lancet*, 1955, **268**, 781.) A clinical trial was carried out on 30 men and 29 women patients with psychoneuroses or personality disorders who showed some symptoms of an obsessive or compulsive kind. The patients were observed for 7 to 18 weeks, during which all received chlorpromazine and an inert placebo, and more than half received no treatment for a week during the trial. In 31 patients treatment began with chlorpromazine while in the remainder the placebo was given first. The initial dosage of the drug was 50 to 75 mg. daily, increased after a week to 100 mg., and after a further week to 150 or 200 mg. at which level it was maintained for the remainder of the course. A significant response to chlorpromazine occurred in 27 of the patients. All had a return of symptoms on replacing the drug by the placebo, usually within 3 to 5 days. 6 patients became considerably worse after the drug was withdrawn than they had been before treatment began; of these, 3 developed a state of agitated depression which necessitated admission to hospital. Of the 32 patients who did not respond to chlorpromazine, 10 showed some improvement but as it continued whether the drug or the placebo was given it was assumed to be spontaneous. After withdrawal of chlorpromazine there was a significantly smaller response to a subsequent course of treatment. In addition to the patients completing the course of treatment, 16 commenced treatment but were not included in the results. Of these, three developed jaundice. Pyrexia sometimes occurred, and 2 patients developed hypnagogic hallucinations. The best results were obtained in patients in whom tension and anxiety were prominent. Little relief of obsessive-compulsive symptoms apart from aggressive urges and hypochondriacal ideas was obtained. It is emphasised that sudden withdrawal of the drug is inadvisable.

H. T. B.

Chlorpromazine, Inhibitory Actions of, on Motor Activity. S. R. Dasgupta and G. Werner. (*Arch. int. Pharmacodyn.*, 1955, **100**, 409.) Chlorpromazine causes a reduction of muscle tone in cats, which is not due to a neuromuscular blocking action but to central depressant action on tone and reflex regulating centres. Experiments in anæsthetised cats show that the effects of cortical stimulation (pericruciate area) are depressed by 0·5 to 1·0 mg./kg. of chlorpromazine and similar results are obtained with 20 to 30 mg./kg. of mephenesin. Stimulation of the cerebellar cortex in decerebrate cats show that 0·5 mg./kg. of chlorpromazine suppresses the postural responses and decreases decerebrate rigidity. Stimulation of suitable areas of the lateral reticular formation (area of the restiform body) show the drug to reduce turning movements. It also reduces the height of the contraction elicited by stimulation of descending medullary tracts, like mephenesin. The crossed extensor reflex of decerebrate cats is completely suppressed by 0·5 mg./kg. of chlorpromazine, and is antagonised by strychnine (20–30 μg.). The crossed extensor reflex of spinal cats is comparatively resistant to the blocking action of chlorpromazine. The results show the close similarity of the inhibitory actions of the drug on motor activity with the effect of a typical "interneuron-blocking" drug mephenesin.

G. F. S.

Chlorpromazine in Mental Hospital Patients. J. Lomas. (*Brit. med. J.*, 1955, **1**, 879.) This is a report on the treatment of 205 patients with chlorpromazine over a period of 4 months. The generally adopted scheme of dosage was to give 50 mg. three times daily orally in the first week, 75 mg. three times daily in the second week, and 100 mg. three times daily in the third and subsequent weeks. Very few patients failed to tolerate this dosage. Some patients received higher dosages than 300 mg. daily, but most patients who improved on the drug did so on 150 mg. daily. The more disturbed and chronic psychotic patients both tolerated higher dosages and required more drug to produce improvement. Treatment was not abandoned as useless in under 2 months and was not usually prolonged beyond 3 months. It was terminated abruptly without any withdrawal effects being noticed in any case. Almost all cases treated were ambulant. Although a few patients complained of slight giddiness, no marked hypotensive effects were observed except in those with cardiovascular disease. The risk of potentiation of sedatives was negligible in normal doses and was noticeable only in those in whom continual narcosis was produced when it was possible to manage with much smaller doses of barbiturates given in association with chlorpromazine than with barbiturates alone. The results in this series suggest that chlorpromazine may prove useful in the treatment of acute states of excitement of all sorts, in neurotics in whom tension or anxiety is a prominent symptom, and in some depressive patients in whom E.C.T. has proved ineffective. The most striking results were obtained in chronic psychotic patients in whom the prognosis would normally be very bad; it enabled a few of these patients to be discharged and many more to make a good hospital adjustment. In chronic patients the chief part played by chlorpromazine was to make possible the rehabilitation of those in whom this was formerly impossible. It would appear that the results of chlorpromazine treatment are almost identical in both inhibited and overactive patients; this suggests that some revision is needed in the conception of the drug as being mainly a symptomatic treatment for excited states. As good results were found after leucotomy as in other chronic patients.

S. L. W.

Desacetylmethylcolchicine in Myeloid Leukæmia. B. J. Leonard and J. F. Wilkinson. (*Brit. med. J.*, 1955, **1**, 874.) 8 patients with chronic myeloid leukæmia were treated with desacetylmethylcolchicine (Colcemid). The initial oral dose of 3 mg. daily was increased after 3 or 4 days to a total of 10 mg. daily according to the white-cell count. This dosage was continued until the leucocytes dropped to approximately 25,000 per cu.mm. and was then stopped for 3 to 4 days. A daily maintenance dose of 3 to 5 mg. was then instituted. Daily white-cell counts, platelet counts and hæmoglobin estimations were performed until the maximal effect on the white cells had been attained; thereafter counts were done twice weekly and finally every 1 to 2 weeks. In 6 of the 8 patients there was distinct clinical improvement; their appetites improved, they gained weight and had more energy; their spleens rapidly decreased in size; there was a dramatic reduction in the white-cell count and an increase in the hæmoglobin content and the red-cell count; the platelet counts were unaffected. These 6 patients have been maintained in satisfactory clinical and hæmatological states for periods of from 4 to 9 months and have carried on with their normal occupations. It appears that the compound is a more selective granulocyte depressant than other chemotherapeutic agents. The disadvantages of myleran in producing thrombocytopenia and aplastic anæmia, and in some cases in precipitating an acute myeloblastic leukæmia, were not seen in this group of cases. In 2 patients with myelofibrosis the white cells were extremely sensitive to Colcemid and dropped to low levels in 3 and 5 days respectively. The results of the treatment in 6 patients with acute myeloid leukæmia were disappointing; in spite of some reduction in the number of myeloblasts clinical deterioration continued and in no case was a remission obtained. The use of Colcemid would appear to be contraindicated in chronic lymphatic leukæmia, and evidence (in one case) suggests that it may even aggravate the condition. S. L. W.

Hydrocortisone, Intravenous, Clinical Uses of. F. Dudley Hart. (*Brit. med. J.*, 1955, **1**, 454.) Intravenous hydrocortisone is available for use in patients suffering from acute adrenal insufficiency when cortisone or hydrocortisone acetate by mouth or by intramuscular or intra-articular injection do not act with sufficient promptness. In Addisonian crisis an intravenous drip of 10 to 20 mg. hydrocortisone for 6 to 8 hours usually effects sufficient improvement to allow of oral or intramuscular therapy. In adrenalectomised patients affected by some additional stress such as infection, intravenous hydrocortisone may be life-saving. Partial adrenal insufficiency may occur as a result of additional stress, such as a surgical operation, in patients being treated with cortisone. Other conditions in which the use of hydrocortisone should be considered include the Waterhouse-Friderichsen syndrome, acute renal insufficiency due to stress in Simmonds's disease, and severe status asthmaticus, acute disseminated lupus erythrematosus and overwhelming allergic reactions. Sodium retention and œdema are not a serious danger during the short periods of treatment needed in adrenal crisis and the hazard is diminished by using 5 per cent. dextrose. The drug is rapidly eliminated and after its use full doses of oral or intramuscular cortisone must be given, or intramuscular cortisone can be given simultaneously. The patients must be closely watched, especially those with metastatic malignant disease who have been adrenalectomised; if signs of post-operative infection are observed antibiotic therapy must be instituted. H. T. B.

Isoniazid in the Treatment of Pulmonary Tuberculosis in Children. R. McL. Todd. (*Lancet*, 1955, **269**, 794.) Isoniazid was administered to alternate

children in a group of 50 with primary pulmonary tuberculosis. Children not given isoniazid received no specific chemotherapy. All were kept in bed for 4 to 8 weeks and were then allowed to return gradually to full activity. Dosage of isoniazid was 3 mg./lb. body weight per day, in 3 doses, for 3 months. Progress was assessed by (1) vitality, appetite and clinical examination; (2) change in body weight; and (3) radiological evidence. Improvement in appetite was seen in almost every treated case. Except in infants under 3 years of age, the increase in body weight was greater in the treated children than in the controls and a statistically significant difference was found in the 3 to 6 year age group. X-ray shadows tended to clear earlier in the treated group but after 1 to 3 years there was little difference in the clinical and radiological condition of the treated and the untreated groups. An impression was formed that the size of the primary lesion decreased more often during the first 3 months in the treated patients. No side effects of isoniazid were observed and the progress made by the patients confirmed previous reports that drug resistance is less likely to occur in children. H. T. B.

Lysergic Acid Diethylamide, Action of, on Mammalian Cholinesterases. R. H. S. Thompson, A. Tickner and G. R. Webster. (*Brit. J. Pharmacol.*, 1955, **10**, 61.) Lysergic acid diethylamide (LSD) caused an increase in acetylcholine levels in the guinea-pig brain (Poloni and Maffezzoni, *Sistema nerv.*, 1952, **4**, 578). In view of this report the authors studied the actions of LSD and other ergot alkaloids on cholinesterases. The enzyme-inhibitory activity was determined manometrically. LSD had relatively powerful inhibitory activity on pseudocholinesterase of human serum and brain, the true cholinesterase and tributyrinase of the brain being only slightly affected by concentrations of LSD which almost completely inhibited the pseudocholinesterase. The inhibition was reversible and competitive in nature. In the rat, guinea-pig, rabbit, chicken and monkey the brain pseudocholinesterase was much less sensitive than was the corresponding enzyme in human brain. 5-Hydroxytryptamine had no effect on the anticholinesterase action of LSD. Ergometrine, methylergometrine, ergotamine, ergotoxine and dihydroergotamine, in decreasing order of activity, all had considerably less action than LSD on human serum cholinesterase.

G. P.

Morphine and Diaminophenylthiazole, Treatment of Intractable Pain with Large Doses of. F. H. Shaw and A. Shulman. (*Brit. med. J.*, 1955, **1**, 1367.) This paper gives a full account of the earlier short report to *Nature* by the authors (*see J. Pharm. Pharmacol.*, 1955, **7**, 431) on the use of diaminophenylthiazole in doses which prevent the respiratory depression and soporific action of morphine, diamorphine and synthetic narcotics without diminishing their analgesic effect. Large, graded doses, up to 2 grains of morphine are given, with 15 mg. of diaminophenylthiazole by intramuscular injection. It is possible in this way to provide 6 to 8 hours of analgesia per dose, and 4 treatments a day may be given so as to obtain continuous analgesia if required. Diaminophenylthiazole has a high therapeutic index, whether used as a morphine antagonist, as a β:β-methylethylglutarimide synergist or in the treatment of barbiturate intoxication. The dose may be increased to as much as 100 mg. if necessary to prevent respiratory depression. Slow and irregular breathing are not signs of respiratory danger, provided that the respirations are deep and cyanosis is absent. Hyoscine, atropine, barbiturates, chlorpromazine and meclozine may be given at the same time. G. B.

Piperazine, *In Vitro* Activity against *Ascaris lumbricoides*. O. D. Standen. (*Brit. med. J.*, 1955, **2**, 20.) Piperazine citrate, adipate and phosphate were tested *in vitro* against *A. lumbricoides* from the pig. All three salts were equally effective in inducing a state of narcosis in the worms. The drug effect was gradual and did not irritate or kill the worms, and when placed in drug-free medium all affected worms recovered in half to two hours. The appearance of worms in the stools of patients treated less than 24 hours previously and the recovery of such worms when placed in warm Ringer solution suggest that the action of piperazine against *A. lumbricoides* in man is very similar to that against *A. lumbricoides* from the pig *in vitro*. It seems almost certain that the worms in the small bowel are likely to be affected 5 to 6 hours after the drug has been given and will remain fully narcotised while a piperazine concentration of 1 : 560 or more persists. Obviously, to achieve successful treatment drug-affected and narcotised worms must be voided in the fæces before the effects of the drug have worn off. In persons with normal bowel movement this can be achieved by a single large dose in the morning, but it is likely that worm clearance would be more certain if the drug was given before the evening meal. In costive patients it would appear desirable that the normal rate of bowel movement should be assisted by a purge timed to take effect within the limits of duration of worm narcosis. S. L. W.

Poliomyelitis Vaccine: American Trials in 1954. (*Brit. med. J.*, 1955, **1**, 1083.) Two distinct but concurrent trials were carried out in areas with a consistently high incidence of poliomyelitis. In one, uninoculated children were used as controls, while in the other the controls were children who were given an injection of something having no influence on immunity to poliomyelitis. In the first study, covering 127 areas in 33 states, 221,998 children received a complete course of vaccinations while the controls numbered 725,173; in the second study, covering 84 areas in 11 states, 200,745 received a complete course while 201,229 were given the placebo injections. Dosage consisted of 3 intramuscular injections each of 1 ml., the intervals between the first and second injections and between the second and third injections being 1 week and 4 weeks respectively. 129 cases of presumed poliomyelitis were reported up to 4 weeks after completion of the course but it is considered that there was no evidence of disproportionate frequency of the disease in vaccinated children. Within a period of 6 to 7 months after vaccination, 1013 children were reported as having poliomyelitis but of these 14·8 per cent. were doubtful or definitely not suffering from that disease, 67·6 had the paralytic form of poliomyelitis and 17·6 per cent. had the non-paralytic form. Of those definitely suffering from poliomyelitis, 79 per cent. had the paralytic form. In the placebo control areas, the ratio of poliomyelitis cases among patients treated with the placebo to those among the vaccinated patients was 2 to 1, and for the paralytic cases 3·5 to 1; on the other hand there was no difference between the two groups in the attack rates of non-paralytic poliomyelitis. Differences between the treated and untreated groups increased with the severity of the disease; there were no fatal cases in the treated groups. Analysis of the results by reference to age showed a significant protective effect against paralytic poliomyelitis for every age except for 6-year-olds, where, based on 16 and 23 cases respectively, the attack rates were 37 and 53 per 100,000 of population in vaccinated and placebo controls respectively. Effectiveness increased with age. The general conclusions were that the vaccine was 80 to 90 per cent. effective against paralytic poliomyelitis; against disease due to Type I virus the effectiveness was 60 to 70 per cent., but

against disease due to Types II and III virus the effectiveness was 90 per cent. or more. H. T. B.

Radioactive Phosphorus in Treatment of Polycythæmia. J. B. Harman, P. L. de V. Hart and E. M. Ledlie. (*Brit. med. J.*, 1955, **1**, 930.) Radioactive phosphorus (^{32}P) is obtained as a solution of orthophosphoric acid and is prepared by the irradiation of sulphur. Its half-life is 14·3 days, but excretion in the urine reduces the effective half-life to 10 days. Phosphorus is largely incorporated into cells in which proliferation is most active, so that ^{32}P provides a method of irradiating the bone marrow in polycythæmia more selectively than can be done by external irradiation. The ^{32}P was given intravenously as sodium phosphate and the patient was discharged from hospital when excretion reached a safe level (100 mC. in 24 hours), usually after 2 to 3 days. At first, in 28 patients, two injections were given, usually of 5 mC. and 4 mC., at intervals of 6 to 12 weeks; subsequently, in 16 patients, a single dose of 4 to 7 mC. was given. There was no obvious difference in the results. The effect on circulating red cells becomes apparent gradually over 2 to 3 months, and the period before improvement occurs can be shortened by massive venesection with simultaneous infusion of a plasma substitute. Observations over a period of up to 6 years show that in most cases the blood concentration can be kept at or near normal and symptoms are relieved, particularly ulceration and sepsis of toes, hæmorrhages, "congested" feelings and enlargement of the spleen. Pruritus may be resistant. Dyspepsia seems to improve except when ulcers are present. The relief lasted for from nearly 1 to over 4 years, with an average of about 2 years; further treatment can then be given. The largest total amount of ^{32}P given to a patient so far is 36 mC. There was no evidence that radiation treatment produced leukæmia or myelosclerosis, both of which may supervene on polycythæmia. ^{32}P may be harmful if leukæmia does develop. H. T. B.

Reserpine and Chlorpromazine, Potentiating Action of. B. B. Brodie, P. A. Shore, S. L. Silver and R. Pulver. (*Nature, Lond.*, 1955, **175**, 1133.) Reserpine and chlorpromazine have both been shown to potentiate the action of hexobarbitone and ethanol on the central nervous system. Mice injected with 100 mg./kg. of hexobarbitone and 5 mg./kg. of chlorpromazine sleep for considerably longer than those given the barbiturate only. Chlorpromazine does not influence the metabolism of the barbiturate, as barbiturate assays of suitably treated homogenates from animals killed at definite times revealed. Furthermore chlorpromazine has no hypnotic action of its own, even in large doses. Finally, animals killed at various times after injections of hypnotics showed no significant difference in the concentration of barbiturate or ethanol in the brain, regardless of whether or not they had also received chlorpromazine. Experiments with reserpine gave similar results and its potentiation of ethanol was striking. The mode of potentiation of hypnotics by SKF-525A is different from that of chlorpromazine and reserpine, since animals recovering from a hexobarbitone hypnosis revert to a deep sleep when treated with chlorpromazine but are not visibly affected when SKF-525A is given intravenously. G. P.

Reserpine Parenterally in Acute Hypertension. F. A. Finnerty, Jr. and J. G. Sites. (*J. Amer. med. Sci.*, 1955, **229**, 379.) Parenteral reserpine was given to 192 hypertensive and toxæmic patients in hospital. The drug was given intravenously or intramuscularly in a dose of 2·5 mg., repeated at 8 to 12 hour intervals if necessary. In addition 47 of the patients received a preparation of veratrum viride intramuscularly and 24 received hydrallazine intravenously. 91 patients showed an average reduction of 23 mm. Hg in systolic and 19 mm.

Hg in diastolic pressure, an effect which lasted an average of 6·5 hours. More striking than the hypotensive effect was the calming influence of reserpine with frequent complete relief of anxiety. As with oral reserpine the greatest use of the drug given parenterally was as background therapy to the more potent hypotensive agents. Though veratrum or hydrallazine was needed to reduce the arterial pressure and control the toxæmic state in 71 patients reserpine enhanced and prolonged the action of these more potent drugs and reduced the dosage requirement, thus greatly reducing the toxicity and making these agents easier to administer. Since reserpine takes 1½ to 2½ hours to exert its effect when given intravenously (3 to 4 hours when given intramuscularly) it should not be relied on as the sole form of therapy in severe toxæmia, particularly in eclampsia. It should not be administered concomitantly with barbiturates since it potentiates their sedative action in some patients. Experience suggests that reserpine is as effective intramuscularly as intravenously and a rational plan of therapy for acute hypertension in the moderately sick patient should consist of reserpine 2·5 mg. intramuscularly every 12 hours, and, if no hypotensive effect is noted after 2 hours, or if the condition becomes worse, give 0·5 mg. of purified veratrum intramuscularly. S. L. W.

Synnematin B in the Treatment of Typhoid. L. Benavides, B. H. Olson, G. Varela and S. H. Holt. (*J. Amer. med. Ass.*, 1955, **157**, 989.) 16 children ranging from 2½ to 11 years of age, suffering from typhoid (12 severe cases and 4 moderate) were treated with the antibiotic synnematin B; all the patients were poorly nourished. There were 6 controls; 3 were untreated, one was treated with tetracycline, one with tetracycline and chloramphenicol, and one with synnematin B on the 26th day of the disease. The dosage of synnematin B was increased gradually as the study progressed as there was no previous dosage experience in human beings with typhoid. Group 1 consisted of 7 patients receiving 80 mg./kg./day body weight (20 mg. of pure synnematin B per kg./day). Group 2 consisted of 4 patients receiving 160 mg./kg./day (40 mg. of the pure drug per kg./day). Group 3 consisted of 5 patients receiving 350 mg./kg./day (87·5 mg. of the pure drug per kg./day). Patients in Group 1 received the drug for 14 days, and patients in Group 2 and 3 for 12 days. Synnematin B was reconstituted with sterile distilled water and given 4-hourly intramuscularly into the buttocks. In all but one case the response to the treatment was similar. Regardless of the day of the disease on which treatment began, the temperature returned to normal, the toxæmia was relieved, the appetite increased, and the mental alertness improved in 2 to 6 days. There was a pronounced improvement in general well-being. In some patients the fever fell by crisis and in others by lysis during the period of treatment, irrespective of the dosage schedule used. The clinical response in Groups 2 and 3 was closely comparable and was far superior to that in Group 1. There were 3 relapses and 1 persistent case, in all of which recovery occurred on further treatment; 2 of the relapses and the persistent case were in Group 1. *Salm. typhi* disappeared from the blood and fæces of every patient during treatment, the organism was recovered from the blood of 3 of the 16 patients after therapy but was never recovered from the fæces of any patient after therapy. This is contrary to the usual experience with chloramphenicol. On the basis of observation in this series it would appear that synnematin B is bactericidal rather than bacteriostatic. Data on blood levels and excretion indicate that the highest levels are attained in 1 hour after injection and that the drug is excreted rapidly by the 4th hour. Urinary concentrations were very high,

(ABSTRACTS *continued on page 792.*)