ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

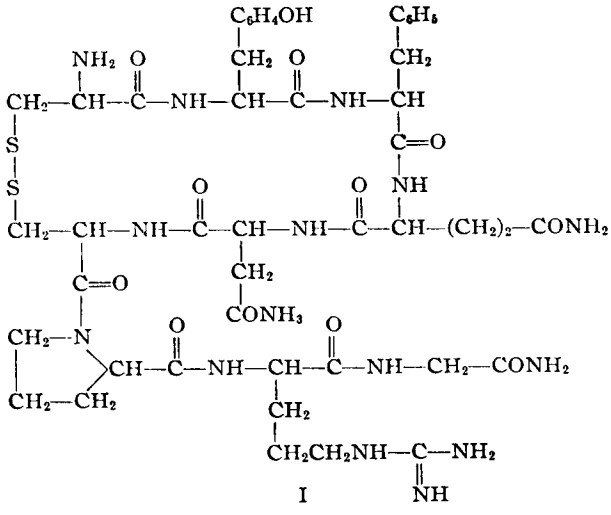
Glyceryl Trinitrate, Determination of, by Nitrite Method. G. Hansen. (*Arch. Pharm. Chem.*, 1958, **65**, 541.) Nitrite is produced when glyceryl trinitrate is decomposed with sodium hydroxide, the quantity obtained being constant even when experimental conditions are varied. Heating 25 ml. of glyceryl trinitrate solution (10 per cent) with 3 ml. of 2N sodium hydroxide in a water bath for 10 minutes, or allowing to stand at room temperature for 1 hour, yields nitrite equivalent to 63·2 per cent of the nitrogen present. The quantity of nitrite in the reaction mixture may be determined by diluting and adding a reagent consisting of ethyl-α-naphthylamine hydrobromide 8 mg., procaine hydrochloride 250 mg., 2N acetic acid 100 ml. The solution is allowed to stand for 30 minutes, and the light absorption measured at 525 mμ. The colour intensity is proportional to the quantity of nitrite in the sample. A correction is made for the nitrite content of the sample, determined separately. This method is stated to be sensitive, reproducible, and specific for alkyl nitrates. Some excipients, such as agar, interfere in the determination, and the alkaline solution must not be heated if lactose is present. G. B.

Papaverine, Colorimetric and Fluorimetric Tests for. H. Wachsmuth and K. Cornelis. (*J. Pharm. belg.*, 1958, **13**, 130.) For colorimetric analysis a sample containing 2 to 15 mg. of papaverine is dissolved in ethanol and diluted to 1·5 ml. 5 ml. of a 0·45 per cent w/v solution of sodium β-naphthaquinone sulphonate in methanol and 1 ml. of pyridine are added and the tube sealed and heated for 2 hours in a boiling water bath. After cooling and extracting with chloroform, an aliquot quantity of the chloroform layer is diluted to 10 ml., dried over anhydrous sodium sulphate, and its optical density at 530 mμ determined against a reagent blank. The quantity of papaverine is calculated from the optical density. Results are satisfactory, and are not affected by the presence of atropine, codeine or phenobarbitone. The suggested fluorimetric method is more sensitive, but the presence of codeine or phenobarbitone may give rise to errors. A sample containing 10 to 100 μg. of papaverine is dissolved in 1 ml. of hydrochloric acid and heated in a stoppered tube for 1 hour in a boiling water bath, cooled in ice, carefully neutralised with ammonium hydroxide solution and diluted to 10 ml. The quantity of papaverine is calculated from the intensity of the strong green fluorescence, measured with a spectrophotometer. G. B.

Quinine from Quinidine, Rapid Chemical Method for Distinguishing. M. Petković. (*Acta Pharm. Jug.*, 1958, **8**, 7.) About 10 mg. of base or salt is placed in a watchglass, and about 1 ml. of ethanol (96 per cent) added. After the solid has dissolved, one drop of dilute sulphuric acid is added and mixed thoroughly with the solution. A drop of solution is placed on filter paper and treated with iodine vapour for 30 seconds. Spots due to quinine appear grey-blue to grey-purple with a dark yellow edge, and those due to quinidine dark yellow, changing to yellow on allowing to stand in the air. G. B.

ORGANIC CHEMISTRY

Arginine-Vasopressin, Synthesis of the Pressor-Antidiuretic Hormone. V. du Vigneaud D. T. Gish, P. G. Katsoyannis and G. P. Hess. (*J. Amer. chem. Soc.*, 1958, **80**, 3355.) Arginine-vasopressin (I) the principal pressor and antidiuretic hormone of the posterior pituitary gland of beef has been



I

synthesised from the protected hexapeptide amide, carbobenzoxy-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-arginylglycinamide. Treatment of this with hydrobromic-acetic acids yielded L-glutaminyl-L-asparaginyl-*S*-benzyl-L-cysteinyl-L-prolyl-L-arginylglycinamide dihydrobromide. This was converted to the monohydrobromide with triethylamine and coupled with the azide of *S*-benzyl-*N*-tosyl-L-cysteinyl-L-tyrosyl-L-phenylalanine to give a crude protected nonapeptide hydrobromide, which on treatment with sodium and liquid ammonia (to remove the protecting groups), and oxidation of the resulting sulphydryl nonapeptide by aeration in dilute aqueous solution pH 6·7, gave the required product. Purification was effected by countercurrent distribution and electrophoresis. The activity of the synthetic product (360–400 units/mg.) is comparable with that of natural arginine-vasopressin. Both natural and synthetic products behaved similarly on countercurrent distribution, paper electrophoresis at two different pH's and on ion exchange chromatography with IRC50. J. B. S.

Sulphanilyl- and Sulphonylcarbamic Acid Derivatives and their Blood-sugar Lowering Activity. E. Haack. (*Arzneimitt.-Forsch.*, 1958, **8**, 444.) The main methods of synthesising these compounds are reviewed and their chemotherapeutic relationships correlating structure with activity, toxicity, length and intensity of effect and metabolic effects. In 13 tables, 133 compounds are characterised, most of which are new. D. B. C.

PHARMACY

Amphetamine Sulphate, *In Vitro* Method for the Determination of the Rate of Release of, from Sustained Release Medication. J. Royal. (*Drug Standards*, 1958, **26**, 41.) The following method was applied to sustained-release capsules

containing amphetamine sulphate in the form of small spherical pellets. A weighed quantity of the pellets was placed in a modified U.S.P. tablet disintegration apparatus, which was operated with 150 ml. of simulated gastric fluid at 37°. Samples were taken at intervals up to 60 minutes, after which the gastric fluid was replaced by simulated intestinal fluid, and samples taken up to 6 hours. Sodium hydroxide was added to the samples, which were then distilled to separate the amphetamine. The amphetamine obtained from gastric fluid samples was determined spectrophotometrically at 257 mμ applying a correction for the absorption due to other substances. With the intestinal fluid samples it was found necessary to remove interfering substances by extraction with ether before determination of the absorption at 257 mμ. The residue remaining on the screen of the disintegration testing apparatus was also distilled with sodium hydroxide and assayed spectrophotometrically at 257 mμ. G. B.

Bactericide: Leukocide Ratio: A Technique for the Evaluation of Disinfectants. L. Greenberg and J. W. Ingalls. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 531.) To determine the toxicity of disinfectants to leukocytes, 0·2 ml. of fresh defibrinated rat blood was mixed with 1 ml. of diluted disinfectant in a centrifuge tube, and allowed to stand at 37° for 10 minutes. About 50 ml. of warm sterile isotonic saline was added and the suspension centrifuged, the supernatant fluid being discarded. A suspension of *Micrococcus pyogenes* var. *aureus* in rat serum was used to test the residue, 0·1 ml. being mixed with the residue and incubated at 37° for 1 hour. A loopful was removed, stained with Wright's stain, buffered with Wright's buffer, washed and examined microscopically for evidence of phagocytosis. The disinfectants were also examined for bactericidal effect, and the ratio of bactericidal to leukocidal concentrations calculated in each case. Under the conditions of the tests, only gentian violet, "Clorax" (a combination of sodium chlorate and sodium metaborate) and povidone-iodine were less toxic to leukocytes than to bacteria. G. B.

Polyvinyl Chloride or Rubber Caps, Stability of Aqueous Solutions in Ampoules and Multiple-dose Containers, Closed by means of. A. B. Nielsen. (*Dansk. Tidsskr. Farm.*, 1958, **32**, 109.) A number of solutions were stored in ampoules, vials closed with rubber caps, and vials closed with "resistant caps" made from polyvinyl chloride backed with rubber. Solutions of sodium aurichloride and potassium permanganate were shown to be most rapidly reduced in the vials closed with rubber caps, and during six months' storage ascorbic acid solutions decomposed to the greatest extent in contact with the rubber caps. In experiments with solutions of adrenaline and sodium nitrite little difference was observed between rubber and polyvinyl chloride caps. "Resistant" caps absorb sodium metabisulphite to a smaller extent than rubber caps, and seem preferable for many solutions. However, they absorb phenol and chlorocresol more readily than rubber caps, and so cannot be recommended for use in the presence of phenolic bacteriostatics. G. B.

Vitamin Preparation, Liquid, An Investigation of the Relative Stability of. J. N. Delgado, F. V. Lofgren and H. M. Burlage. (*Drug Standards*, 1958, **26**, 51.) Multivitamin solutions containing aneurine, ascorbic acid, nicotinamide, riboflavine-5-phosphate sodium, panthenol, pyridoxine hydrochloride, vitamin B_{12}, folic acid and vitamins A and D were prepared in a vehicle containing water 20 per cent, with either propylene glycol 80 per cent or

propylene glycol 40 per cent and glycerin 40 per cent. Some solutions containing a greater proportion of water were made, and in some cases aneurine nitrate was used instead of the hydrochloride. The solutions were assayed for aneurine, ascorbic acid, riboflavine, pyridoxine, nicotinamide and vitamin A, stored at 47° for 30 days, and again assayed. It was shown that increasing the proportion of water decreased the stability of aneurine, both hydrochloride and nitrate. Aneurine nitrate was more stable in the vehicle containing 80 per cent of propylene glycol, and the hydrochloride was more stable in that containing 40 per cent each of glycerin and propylene glycol. The addition of disodium calcium edetate and ethyl hydrocaffeate appeared to improve the stability or ascorbic acid. A vehicle containing disodium calciumedetate 0·01, ethyl hydrocaffeate 0·05, water 20 and propylene glycol 80 was found to be the most satisfactory. The method of preparation of the multivitamin solution is described in detail, and the following percentages of excess should be added to provide for a shelf-life of 2 years; aneurine nitrate 55, riboflavine-5-phosphate sodium 33, ascorbic acid 23, pyridoxine hydrochloride 16, nicotinamide 20, and vitamin A 16. G. B.

PHARMACOLOGY AND THERAPEUTICS

Captodiame, Investigation of the Mechanism of its Potentiating Effect on Hexobarbitone. I. Eberholst, I. Huus and R. Kopf. (*Arzneimitt.-Forsch.*, 1958, **8**, 379.) Captodiame, like iproniazid, appears to potentiate hexobarbitone by inhibiting its metabolism. Thus if mice were given captodiame (20 mg./kg.) followed in 30 minutes by hexobarbitone, and the latter analysed after a further 10, 15, 30 and 60 minutes, the concentration of hexobarbitone was significantly higher than that in mice which had not received the captodiame. At the time of awakening from anaesthesia, however, the concentration was the same in the two groups. *In vitro* experiments with liver slices suggested that captodiame had an inhibitory effect on the metabolism of hexobarbitone. Chlorpromazine was also tested for its effect, and was found to be a much more powerful potentiator of hexobarbitone. It appeared to have no effect on the metabolism of hexobarbitone, and thus acted by a different mechanism. D. B. C.

Cascara, Chronic Potassium Depletion due to. B. J. Houghton and M. A. Pears. (*Brit. med. J.*, 1958, **1**, 1328.) This is a report of a case of chronic potassium depletion in a woman of 55. In addition to anorexia, dryness of the mouth, thirst, and general weakness, her legs became so weak that she was unable to lift them or to flex her hips. For at least five years previous to admission she had habitually taken 10–15 grains of cascara, two or three times a week. Replacement of potassium by intravenous drip, using 4 g. of potassium chloride in a litre of 5 per cent dextrose in water, produced a dramatic improvement within 24 hours, and she made an uneventful recovery. The results of balance studies carried out over a nine-day period are reported. Over the 9 days from the beginning of treatment the patient gained a total of 796 mEq. of potassium and lost 376 mEq. of sodium, without concomitant changes in weight.

S. L. W.

Chlorothiazide: Clinical and Laboratory Studies. W. C. Watson, T. J. Thomson and J. M. Buchanan (*Lancet*, 1958, **1**, 1199.) A study of the clinical and biochemical effects of a single oral dose of chlorothiazide 2 g., given to 22 patients with various "water-retaining" conditions, showed it to be an

effective and safe oral diuretic, which acts principally by promoting excretion of sodium and chloride, but in certain circumstances by promoting excretion of potassium and bicarbonate. In general, the best diuretic response occurred in the type of patient who responds well to mersalyl. In patients with pulmonary heart-disease the response was disappointing. It is doubtful whether a regimen of divided doses (i.e., 1 g. twice daily) has any clinical advantages; unless there are urgent reasons for obtaining a maximal diuresis, single doses are preferable, as they avoid the fatigue of unnecessary nocturia. S. L. W.

Chlorothiazide, Diuretic Action. N. A. Matheson and T. N. Morgan (*Lancet*, 1958, **1**, 1195.) In trials on 10 healthy men, chlorothiazide, in a dose of 2 g. by mouth was shown to be an effective diuretic. The diuretic effect appeared within 2 hours, was well maintained over the first 8 hours, and then subsided but was not quite complete by 12 hours. During the second 12-hour period the excretion-rates returned to control values. With intravenous injection of 500 mg. of the sodium salt, the changes were maximal within the first hour, and the effect lasted about 4 hours. Compared with acetazolamide 0·5 g., chlorothiazide 2 g. is a less potent carbonic-anhydrase inhibitor, hence recovery of base is more rapid. The action of chlorothiazide is likely to be maintained and because of this it may induce hypopotassaemia. S. L. W.

5-Hydroxytryptamine in Tissues, Turnover of. S. Udenfriend and H. Weissbach. (*Proc. Soc. exp. Biol. N.Y.*, 1958, **97**, 748.) Although the bulk of 5-hydroxytryptamine is present in the mucosa of the gastrointestinal tract, significant amounts are also found in blood platelets, brain, spleen and lung. Enzymes involved in 5-hydroxytryptamine formation and destruction are present in all depots except blood platelets, indicating that the amine is apparently made, released and destroyed for specific functions in these depots. In this paper a study is made of the rate of turnover of 5-hydroxytryptamine in various tissues in order to help in the elucidation of these functions. Using tryptophan-^{14}C and 5-hydroxytryptophan-^{14}C it was possible to measure the turnover of 5-hydroxytryptamine in a number of tissues of the rabbit. The half-lives were found to be: platelets and spleen, 33–48 hours; stomach, 17 hours; intestine, 11 hours. Although amounts of 5-hydroxytryptamine in the brain were too small to permit isotopic measurement, it was possible to estimate its turnover from the increase following the administration of harmaline, an inhibitor of 5-hydroxytryptamine metabolism. Such estimates indicated a half-life of the order of minutes. M. B.

Iproniazid, Effect of, on Brain Levels of Noradrenaline and Serotonin. S. Spector, D. Prockop, P. A. Shore and B. B. Brodie. (*Science*, 1958, **127**, 704.) It is known that iproniazid inhibits monoamine oxidase, an enzyme which can inactivate noradrenaline and serotonin—substances present in the brain. Monoamine oxidase plays a major role in the physiological inactivation of both these amines in the brain. The data presented in this paper show that repeated doses of iproniazid induce a marked rise in the brain levels of both noradrenaline and serotonin, together with signs of central stimulation. However, it is not possible to conclude that the central stimulant effect of iproniazid is causally related to the increase in brain amines. Nevertheless it is significant that the administration of large doses of 3:4-dihydroxyphenylalanine, a noradrenaline precursor, or of 5-hydroxytryptophan, a serotonin precursor, causes central excitation which is enhanced by pretreatment with iproniazid. M. B.

(+)-Lysergic Acid *cyclo*Alkylamides. Pharmacology of. Z. Votava, I. Podvalová and M. Semonský. (*Arch. int. Pharmacodyn.*, 1958, **115**, 114.) Five (+)-lysergic acid *cyclo*alkylamides, i.e. *cyclo*propyl-, *cyclo*butyl-, *cyclo*pentyl-, *cyclo*hexyl- and *cyclo*heptylamide were synthesised and their pharmacological activity was compared with that of (+)-lysergic acid diethylamide and ergometrine. The *cyclo*butyl and *cyclo*pentyl derivatives showed marked oxytocic, antiserotonic and mydriatic effects, while the others were less active. All of the drugs were equipotent in producing a rise in the body temperature of rabbits and a rise followed by a prolonged fall in mice. Blood pressure was hardly affected in anaesthetised rabbits and dogs and in unanaesthetised dogs. Toxic doses produced central effects similar to those of amphetamine. Preliminary clinical tests confirmed that the substances produced oxytocic effects without any hallucinogenic action. W. C. B.

Methocarbamol in Neuromuscular Disease. H. W. Park. (*J. Amer. med. Ass.*, 1958, **167**, 168.) Methocarbamol was evaluated in 42 patients with a variety of disorders manifesting an increase in involuntary muscle tone. In 30 patients with pyramidal tract and acute myalgic disorders, use of the drug resulted in a significant improvement in 27 (90 per cent), questionable improvement in 2, and none in 1. There was no change in 12 patients with chronic arthritic, extrapyramidal and myalgic disorders. Good results were obtained in patients with acute low back pain and acute torticollis. All patients who had a demonstrable effect to the medication attained the effect within 30 to 45 minutes after intravenous administration (0·5 to 1 g.), or within 72 hours on oral medication (1 to 2 g. four times daily). Side-effects were negligible and were reversed on slight reduction of dosage. S. L. W.

Normorphine, Human Pharmacology and Addiction Liability of. H. F. Fraser, A. Wikler, G. D. Horn, A. J. Eisenman and H. Isbell. (*J. Pharmacol.*, 1958, **122**, 359.) Other workers have suggested that normorphine, a possible metabolite of morphine, may be an effective analgesic but showing little evidence of physical dependence. Therefore a study has been made of its pharmacology and its addiction liability. It was found that in single doses normorphine caused less sedation, less depression of temperature, less respiratory depression and less pupillary constriction than did equal doses of morphine. Administration of 9 to 10 mg. of normorphine every six hours for seven doses caused less, but longer lasting, pupillary constriction than did equal doses of morphine. Cumulation of the sedative effects of normorphine occurred in this experiment. When normorphine was substituted for morphine in addicted patients it completely supressed the morphine abstinence syndrome. The intensity of abstinence observed after withdrawal of normorphine was far less than the intensity of abstinence from morphine. Marked cumulation of sedative effects occurred during direct addiction to normorphine and prevented raising the dose to the level which could easily have been attained with morphine. Partial tolerance to the sedative effects developed. Nalorphine precipitated definite abstinence syndromes in patients addicted to normorphine. The intensity of abstinence after the withdrawal of the normorphine was slow in onset and milder than abstinence from morphine, methadone or codeine. The urinary excretion of 17-hydroxycorticosteroids was depressed during chronic administration of normorphine and elevated transiently after the normorphine was discontinued. These results suggest that the practical addiction liability of normorphine is low. M. B.

Pempidine in the Treatment of Hypertension. M. Harington, P. Kincaid-Smith and M. D. Milne. (*Lancet*, 1958, **2**, 6.) Pempidine is a ganglion-blocking agent closely resembling mecamylamine in its properties. It may be used orally as the bitartrate, which contains about 50 per cent of the active base, or intravenously as the hydrochloride, which contains about 80 per cent. As it is freely absorbed from the gut, the oral form will usually be preferred. Both drugs are excreted more rapidly in acid than in alkaline urine, are concentrated in tissue containing a high proportion of cell nuclei, and easily cross the blood-brain barrier. There are, however, important differences which may make pempidine a more useful antihypertensive agent than mecamylamine. The excretion of pempidine is more rapid and is less affected by variation in acid-base balance than that of mecamylamine and allows the dosage of pempidine to be quickly increased; the hypotensive effect of pempidine is less variable. The effective dosage of pempidine in hypertension in man is usually lower than that of mecamylamine; side-effects will probably be less severe and briefer. From a clinical trial on 27 patients with hypertension who received continuous treatment with pempidine over periods varying from 2–20 weeks it was shown that a steady hypotensive effect can be maintained throughout the day when pempidine is given orally at 5-hourly intervals. The initial dose was usually 2·5 mg. given four times daily, and this was raised rapidly by increments of 2·5 mg. daily until an adequate hypotensive effect was achieved. The effective dose varied widely but the average total given as maintenance treatment was 32·5 mg. bitartrate (16 mg. base). There was no evidence of the development of tolerance. Most of the patients experienced some side-effects similar to those observed with other ganglion-blocking agents. The most frequent symptoms were constipation, dryness of the mouth, and blurring of vision. All side-effects (including a syndrome of early paralytic ileus in 3 patients) disappeared rapidly on stopping the drug. S. L. W.

Pyridine-2-aldoxime Methiodide Therapy for Alkylphosphate Poisoning. T. Namba and K. Hiraki. (*J. Amer. med. Ass.*, 1958, **166**, 1834.) Pyridine-2-aldoxime methiodide (PAM) is a specific reactivator of alkylphosphate-inhibited acetylcholinesterase and produces a prompt and complete relief of symptoms due to poisoning with insecticides such as parathion. For this purpose it completely replaces atropine. Cholinesterase activity of red blood cells is restored instantly and completely recovers; that of the serum recovers only transiently. It has no influence on the cholinesterase activity of normal blood. One intravenous injection of 1 g. of PAM is usually sufficient, but the dose may be repeated or increased if necessary. No serious side-effects have been encountered even with large doses. If given in sufficient dosage the effect, even of a single injection, is dramatic, with prompt recovery of clear consciousness, disappearance of muscular fasciculations, and improvement of respiratory function. The successful treatment of five serious cases of parathion poisoning due to spraying is reported. S. L. W.

Pyrogen, Endogenous, Role of, in the Genesis of Fever. W. B. Wood, Jr. (*Lancet*, 1958, **2**, 53.) Evidence is presented that endogenous pyrogen derived from polymorphonuclear leucocytes in inflammatory exudates is one of the factors responsible for many kinds of fever. Leucocytes have been shown to be the principal source of endogenous pyrogen in granulocytic exudates, and to discharge pyrogen into the surrounding medium while still motile and functionally active. The pyrogen acts directly on the thermoregulatory centres

of the brain. Its chemical constitution has not been elucidated, but it differs from bacterial pyrogens, pyrexin, and pyrogenic polysaccharides in being inactivated on heating to 90° for 30 minutes, non-dialysable through Cellophane, resistant to the action of trypsin, chymotrypsin, and ribonuclease, and unaffected by changes in pH from 2·0–10·5. It is possible that cells other than polymorphonuclear leucocytes may be able to produce similar pyrogenic factors. G. B.

Piperazine, Action of, on *Necator, Trichuris* and *Strongyloides*. J. A. McFadzean and S. R. Smithers. (*Trans. R. Soc. trop. Med. Hyg.*, 1958, **52**, 235.) Five cases each of infestation with *Necator americanus*, *Trichuris trichiura* and *Strongyloides stercoralis* were treated with piperazine adipate. For *Trichuris* infestation a single dose of 3 g. was given, followed by 0·6 g. thrice daily for 5 days, while for *Strongyloides* 0·6 g. was given 5 times daily for 5 days. The drug appeared to have no action on either *Trichuris* and *Strongyloides*. Three patients with *Necator* infestation were given a single dose of 2·4 to 3 g., a fourth patient was given 3 g., followed after 2 days by 3·6 g., and a fifth patient was given 3 g., followed on the 3rd and 5th days by 3·6 g. It appeared that piperazine had some effect on the infestation, but that repeated doses were necessary to achieve significant diminution in the number of parasites.

G. B.

Polybactrin Aerosol in Prophylaxis of Surgical Sepsis. R. M. Gibson. (*Brit. med. J.*, 1958, **1**, 1326.) A clinical trial is reported in which Polybactrin Aerosol applied locally to wound surfaces was used in 250 consecutive neurosurgical operations. Polybactrin is a mixture of polymyxin, bacitracin and neomycin for local use. The difficulties associated with its relative insolubility and instability in aqueous solutions have been overcome by suspending the mixture in an inert, highly volatile anhydrous liquid "dichloro-tetrafluoro ethane". The wound was sprayed at each wound layer encountered on opening and closure. The results were contrasted with a comparable series in which the antibiotic technique was not used. The analysis showed a reduction in the incidence of major sepsis from 7·2 to 0·4 per cent, and in minor sepsis from 1·2 to 0·8 per cent. S. L. W.

Quinalbarbitone in Pre-anaesthetic Medication. J. E. Eckenhoff and M. Helrich. (*J. Amer. med. Ass.*, 1958, **167**, 415.) A blind study of morphine, pethidine, alphaprodine, quinalbarbitone, and saline solution as pre-anaesthetic medicaments was made in 1400 surgical patients. The solutions of narcotics and of quinalbarbitone were prepared so as to provide equipotent doses of each of the drugs per ml. (in the case of quinalbarbitone the dose was 75 mg./ml.). All the injections were given intramuscularly and all were given in combination with atropine sulphate. The results showed that the use of quinalbarbitone led to a higher proportion of alert and awake patients, free from apprehension, than did the narcotics. The narcotics produced more drowsy or sleepy patients, but also a higher incidence of apprehension; they also produced more undesirable side-effects than quinalbarbitone. Respiratory depression was more common with the narcotics. When narcotics had been used pre-operatively the patients remained narcotised longer after anaesthesia than did those who received quinalbarbitone or saline solution, but they did not complain so much of pain or appear so restless as did the latter group. The authors suggest that the continued routine use of narcotics for pre-anaesthetic medication is unwise and unwarranted. S. L. W.

Triamcinolone in the Treatment of Psoriasis. W. B. Shelley, J. S. Harun and D. M. Pillsbury. (*J. Amer. med. Ass.*, 1958, **167**, 959.) Sixty patients with psoriasis were treated with triamcinolone in doses of 12–16 mg. daily by mouth. In 36 of the patients there was a prompt and undoubted response; within a week the scaling and erythema diminished significantly, and within two to four weeks of continued treatment the psoriasis was in some patients completely cleared up, though on cessation of treatment or reduction of dosage the lesions regularly returned. The remaining 24 patients failed to show any response. A wide variety of reversible side-effects were observed. Some were favourable, such as the stimulation of hair-growth in alopecia areata, and many were unfavourable, such as flushing, hyperhidrosis, facial hirsutism and facial contour changes. The treatment should be reserved for acute extending psoriasis not controllable by other means or for very extensive and severe chronic psoriasis. Topical triamcinolone therapy was found to be without effect. S. L. W.

Triamcinolone in the Treatment of Rheumatoid Arthritis. E. F. Hartung. (*J. Amer. med. Ass.*, 1958, **167**, 973.) Sixty-seven patients with rheumatoid arthritis were treated with triamcinolone (free alcohol form). The initial dose was usually 24 mg. a day, given in four divided doses, the average maintenance dose being 10 mg. daily in four divided doses. In 23 of the patients the drug was stopped within six months owing to side-effects. Of 23 treated for six months up to 11 months the therapeutic results were good in 16. In the treatment of rheumatoid arthritis the drug appears to have four important advantages over other steroids: (1) lack of production of oedema; (2) fewer gastrointestinal symptoms, especially the peptic ulcer syndrome; (3) less psychic irritation; and (4) no effect on arterial blood pressure. Nevertheless, it retains many of the disturbing side-effects of the other corticosteroids, particularly the masculinising effects, facial rounding, cutaneous purpura or ecchymosis, and acne. Increased sweating and leg cramps were prominent. S. L. W.

Warfarin as an Anticoagulant. S. Baer, M. W. Yarrow, C. Kravitz and V. Markson. *J. Amer. med. Ass.*, 1958, **167**, 704.) The anticoagulant effects of warfarin and dicoumarol were compared in 200 patients, suffering from acute myocardial infarction or severe coronary insufficiency. Warfarin was given orally to 164 patients, the prothrombin times being determined daily. Individual dosages were adjusted until the daily dose (usually 5–7·5 mg.) needed to maintain the prothrombin level between 15 and 30 per cent was found. Dicoumarol was given to 19 patients and dosages similarly adjusted until the maintenance dose (between 20 and 100 mg. daily) was found. An additional group of 17 patients, started on dicoumarol therapy, were later transferred to warfarin. Of all patients receiving warfarin, 87 per cent reached true therapeutic levels within 48 hours, and 83·5 per cent were within therapeutic range 70 per cent of the time or more. With dicoumarol, only 33·3 per cent of the patients were within therapeutic range for 70 per cent of the time. Warfarin was found easy to use, and prothrombin times were smoothly and easily controlled with small daily maintenance doses. There were no important side-effects. The authors conclude that warfarin is far superior to dicoumarol as an anticoagulant, and most closely approaches the "ideal anticoagulant." S. L. W.