ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Colchicine, Radioactive, Biosynthesis and Isolation of. E. J. Walaszek, F. E. Kelsey and E. M. K. Geiling. (*Science*, 1952, **116**, 225.) *Colchicum autumnale* corms were allowed to develop 5 to 8 inches of leaf growth and then were placed in a sealed growing chamber into which radioactive carbon 14 was introduced in the form of carbon dioxide. After 20 to 30 days the corms were sliced, dried, powdered and extracted with methanol, the crude colchicine product dissolved in benzene and chromatographed upon alumina to give a yield of 0·1 to 0·2 per cent. of almost colourless colchicine. Colchicine was also isolated from the leaves of radioactive *Colchicum autumnale* in 0·04 to 0·08 per cent. yield. The radioactive colchicine was identified by comparison with a purified U.S.P. sample of colchicine. In this comparison, melting points, optical rotations, ultra-violet absorption spectra, polarographic reduction, paper chromatography and colour reactions were applied and recorded. In addition to colchicine, 5 other related alkaloids from *Colchicum autumnale* were isolated in a radioactive condition. A. H. B.

Germbudine, *iso*Germidine and Veratetrine. Three New Alkaloids from *Veratrum viride*. G. S. Myers, W. L. Glen, P. Morozovitch, R. Barber and G. A. Grant. (*J. Amer. chem. Soc.*, 1952, **74**, 3198.) From the alkaloids extractable from the ground roots and rhizomes of commercial *Veratrum viride* have been obtained germerine and three new, highly potent, ester alkaloids for which the names germbudine, *iso*germidine and veratetrine are proposed. The benzene-extractable alkaloids were separated into a crystalline non-ester alkaloid fraction and an amorphous fraction which contained the bulk of the hypotensive activity. This amorphous material was subjected to a 24-plate Craig counter-current distribution between benzene and 2M acetate buffer at *p*H 5·5 and the known triester neogermitrine obtained. Subsequent 72-plate Craig distribution of the alkaloids from tubes 0–3 from the above, using benzene and 2M acetate at *p*H 6·5, gave the three new alkaloids. Germbudine ($C_{37}H_{59}O_{13}N$) afforded the alkamine germine and an acid fraction upon alkaline hydrolysis. *iso*Germidine ($C_{34}H_{53}O_{10}N$), a diester, yielded germine, α-methylbutyric acid and acetic acid upon hydrolysis. Veratetrine ($C_{43}H_{64}O_{16}N$) upon alkaline hydrolysis, yielded *iso*protoverine, α-methylbutyric acid, acetic acid and an unidentified acid identical with one obtained by hydrolysis of germbudine. A. H. B.

ANALYTICAL

Digitalis Glycosides; Detection on Paper Chromatograms. D. Lawday. (*Nature, Lond.*, 1952, **170**, 415.) Antimony trichloride in chloroform reacts with less than 0·5 μg./cm. of glycoside, giving permanent and distinctive colours in visible and ultra-violet light while the background remains unaffected. For the chromatographic development the glycoside solution is applied to the starting line with a micrometer pipette in a spot not more than 0·5 cm. in diameter. The chromatogram is then developed until the solvent front has run 30 cm. The

dried chromatogram is treated with a 20 per cent. solution of antimony trichloride in dry, ethanol-free chloroform, and the paper heated for 3 to 5 minutes at about 70° C. The colours produced are shown in the accompanying table.

Glycoside	Visible		Ultra-violet light	
	Colour	Sensitivity	Colour	Sensitivity
Digitoxin	Red-mauve changing to blue-grey	0·75 μg.	Red	0·25 μg.
Gitoxin	Mauve changing to grey	0·75 μg.	Apple-green	0·25 μg.
Digitoxigenin	Pale turquoise blue	1·0 μg.	Negative	—
Gitoxigenin	Bright orange-yellow	0·75 μg.	Bright orange	0·25 μg.

On heating, the colour due to gitoxigenin appears first, followed by digitoxin, gitoxin, and lastly digitoxigenin, which is least sensitive to the test. S. L. W.

p-Hydroxybenzoyl Esters, Chromatographic Separation and Determination of Mixtures of. T. Higuchi, K. P. Patel, E. R. Bonow and J. Landsman. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 293.) *p*-Hydroxybenzoate esters used as preservatives may be extracted from pharmaceutical mixtures with ether or chloroform. The various esters may be completely separated by partition chromatography on a silicic acid column containing methanol-water mixture as the internal phase, and changing the composition of the external phase gradually from 60 parts (by volume) of Skelly-C with 40 of carbon tetrachloride through carbon tetrachloride to chloroform. The first fractions contain the butyl, and later ones the propyl, ethyl and methyl esters. Mixtures of methyl and propyl *p*-hydroxybenzoates are readily separated by elution with carbon tetrachloride-Skelly-B followed by chloroform. The quantity of ester in an eluted fraction may be determined by evaporating *in vacuo*, dissolving the residue in ethanol, adding 2 drops of 0·2N sodium hydroxide to convert the substance to the phenolate, and measuring the absorption at 301 mμ. G. B.

Khellin, Identification Tests for. H. Laubie. (*Bull. Soc. Pharm. Bordeaux*, 1952, **90**, 108.) The following are recommended. (1) Place a few mg., or 0·2 ml. of the solution for injection, in a porcelain dish with 1 to 2 ml. of ethanol and 0·2 to 0·4 ml. of sodium hydroxide solution, heat on a boiling water bath, and stir and aerate the solution as much as possible. On the surface of the dish an intense pink coloured deposit is formed, which, after evaporating almost to dryness, is soluble in ethanol. This reaction is sensitive to 0·2 mg. of khellin. Tablets may be extracted with ethanol and the filtrate submitted to the test. (2) Ethanolic solutions may be identified by the Legal test. To 1 ml. of the ethanolic solution add 0·1 ml. of sodium nitroprusside solution (5 per cent.) and 0·1 ml. or sodium hydroxide solution; the liquid turns orange. After 2 to 5 minutes add 0·2 ml. of acetic acid; a purple-red colour is produced. G. B.

Malonylurea Derivatives, Infra-red Absorption Spectra of. C. J. Umberger and G. Adams. (*Analyt. Chem.*, 1952, **24**, 1309.) The infra-red absorption spectra of 20 derivatives of malonylurea are recorded and the spectra are examined with a view to classifying the characteristic absorption bands for various groups of compounds. The sensitivity for detection by infra-red was considerably less than in other analytical procedures, between 10 and 30 mg./ml.

of solvent being required and the value of the technique in toxicological work is limited to those drugs which can be recovered in adequate amounts from tissues. Barbiturates and related compounds show infra-red absorption characteristic for the malonylurea structure and, in acute poisonings, recovery of the compounds from the organs is adequate for the analysis. Their chemical structures are closely related, so that the general absorption pattern is typical for the group but minor differences in the spectra can be used to identify individual compounds when absorption data are utilised in conjunction with micro melting points. Controlled concentration is essential for the identification of individual members of a series, since the ratios of the extinctions at two wavelengths may vary appreciably with the changes in concentration in the solvent; it is therefore necessary to run a series of absorption curves on the unknown, starting with a concentrated solution of the drug and then diluting down in steps until optimum extinction is obtained. R. E. S.

***iso*Nicotinyl Hydrazide, Identification Tests and Assay for.** H. Laubie. (*Bull. Soc. Pharm. Bordeaux*, 1952, **90**, 106.) *iso*Nicotinyl hydrazide may be identified as follows. Dissolve 100 μg. in 1 ml. of water and add 0·1 ml. of sodium nitroprusside solution (5 per cent.), 0·1 ml. of caustic soda solution and 0·1 ml. of acetic acid. An intense orange colour is produced (Legal reaction). On the addition of hydrochloric acid the colour changes to green. In alkaline solution, potassium ferricyanide oxidises the hydrazide quantitatively. The substance may be assayed by measuring the nitrogen evolved or the ferrocyanide formed, or more simply as follows. Mix 10 ml. of standard solution of *iso*nicotinyl hydrazide (0·1 per cent. w/v) with 1 ml. of 10N sodium hydroxide and add, drop by drop, a 10 per cent. solution of potassium ferricyanide until a clear yellow colour persists. Carry out the same procedure with 5 to 50 mg. of the sample under test, and calculate the content of *iso*nicotinyl hydrazide. If less than 10 mg. is present in the sample taken, a correction for the volume of potassium ferricyanide solution required to colour a mixture of 10 ml. of water and 1 ml. of sodium hydroxide solution is applied. Tablets containing 50 mg. of *iso*nicotinyl hydrazide may be extracted with a few ml. of water, filtered and the assay performed on an aliquot part of the filtrate. G. B.

***iso*Nicotinyl Hydrazide, Properties of.** A. Engelund, P. Terp and C. Trolle-Lassen. (*Arch. Pharm. Chemi*, 1952, **59**, 560.) The authors give a summary of the information available regarding *iso*nicotinyl hydrazide, from which the following points are taken. The absorption curve shows, in neutral solution, a clear maximum at 262 mμ ($E^{1\ per\ cent.}_{1\ cm.} = 0{\cdot}308$); in 0·1N hydrochloric acid at 266 mμ ($E^{1\ per\ cent.}_{1\ cm.} = 0{\cdot}396$); while in 0·1N sodium hydroxide there is no clear maximum. In presence of 1 molecule of hydrochloric acid the colour of the solution is yellow, the extinction rising rapidly at short wave lengths: this solution again becomes colourless when the proportion of hydrochloric acid is doubled. The following points are taken from a suggested monograph for the compound. M.pt (corr.) 169·5° C. to 172·5 C. Extinction $E^{1\ per\ cent.}_{1\ cm.}$ at 234 mμ = 212 to 219 (minimum) and at 266 mμ = 386 to 398 (maximum). *Identification*: 5 ml. of a 5 per cent. aqueous solution gives with 1 ml. of 2N hydrochloric acid a yellow colour which practically disappears on the addition of a further 2 ml. of acid. If 2 ml. of a 5 per cent. solution is allowed to stand for a short time with a solution of 0·1 g. of vanillin in 10 ml. of warm water, the precipitate obtained, after recrystallisation from diluted ethanol, melts at 228 to 230° C. *Assay*: 0·05 g. is dissolved in 50 ml. of water in an iodine value flask and treated with 1 g. of sodium bicarbonate and 25 ml.

of 0·1N iodine solution. After 15 minutes, 25 ml. of 2N hydrochloric acid is added and the solution is titrated with 0·1N thiosulphate solution. From 97·5 to 100·5 per cent. should be indicated (1 ml. of 0·1 N iodine corresponds to 0·003429 g. of *iso*nicotinyl hydrazide). The compound is soluble in 8 parts of water, and is incompatible with acids, bases and oxidising agents. Sterilisation by heating for 30 minutes at 120° C. has been recommended, but there is some doubt as to the permissibility of this procedure, and it is advisable that solutions should be prepared aseptically. Absorption of the compound, administered perorally, is rapid, the maximum blood concentration being attained after 1 to 2 hours; excretion is through the kidneys. G. M.

Oxalic Acid, Permanganate Titration of. G. E. Mapstone and J. W. Smith. (*Chem. Ind.*, 1952, 856.) It was found that, in the presence of ferrous sulphate, oxalic acid was also quantitatively titrated by permanganate in acid solution at room temperatures. The influence of a ferric salt was examined and it was found that the addition of 5 ml. of 0·1M ferric alum to 20 ml. of 0·1N oxalic acid enabled a permanganate titration to be carried out accurately and quantitatively at room temperature (25° C.). It is suggested that this technique may be used for the titration of oxalic acid without heating. The times taken for the discharge of colour of a potassium permanganate solution by oxalic acid in the presence of ferrous ammonium sulphate at 30° and 1° C. were recorded; the relative constancy of the ratio of the times at 1° C. and 30° C. suggested that both in the presence and absence of the iron salt the same reaction was involved. R. E. S.

Streptomycin and Dihydrostreptomycin, Colorimetric Determination of. F. Monastero. (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41**, 322.) The following determination is based upon the orange-red colour obtained from streptidine with sodium nitroprusside and sodium ferricyanide in alkaline solution. Prepare a reagent by mixing equal volumes of 10 per cent. solutions of sodium nitroprusside, sodium ferricyanide and sodium hydroxide, allowing to stand for 15 minutes and diluting 1·0 ml. to 100 ml. To 10 ml. of an aqueous solution containing 200 to 1000 μg. of streptomycin or dihydrostreptomycin add 10 ml. of reagent and allow to stand for 3 minutes. Determine the absorption with a 490 mμ filter, against a reagent blank prepared with water instead of the streptomycin solution. Calculate the concentration from a standard curve plotted from measurements of the absorption of standard dihydrostreptomycin solutions, similarly treated. Beer's law applies over the range of concentrations used. The colour is stable for 30 minutes and the reproducibility is within 2 per cent. Methanol and sodium chloride interfere. Streptidine also interferes but is generally removed during manufacture. G. B.

ORGANIC CHEMISTRY

Desmethylkhellin and Derivatives. H. Abu-Shady and T. O. Soine. (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41**, 325.) Demethylation of one of the methoxyl groups of khellin was accomplished by heating under a reflux condenser with hydrochloric, hydrobromic or hydriodic acid. The product, desmethylkhellin gave an intense green colour with ferric chloride solution, but was sparingly soluble in sodium hydroxide solution. The foregoing, together with the difficulty in methylating the substance with diazomethane was suggestive of hydrogen bonding with the adjacent carbonyl group, indicating that demethylation had occurred at carbon atom 5, not 8. Methylation with diazomethane

or methyl iodide produced khellin. The acetyl derivative was obtained by heating under a reflux condenser with acetic anhydride and sodium acetate. The ethyl, propyl, butyl, allyl, carbethoxymethyl, acetamido, phenacyl and β-diethylaminoethyl derivatives were made by heating the halide under a reflux condenser with desmethylkhellin in acetone in the presence of potassium carbonate. The carboxymethyl derivative was prepared by hydrolysis of the carbethoxy compound. These substances are being tested pharmacologically. G. B.

Gentisic Acid, a Physicochemical Study of. A. Osol and L. J. Kleckner (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41**, 306.) Pure gentisic acid has m.pt. 201·5° C. (electric hot stage), 201·2° C. (capillary tube). The solubility at 25° C. is 2·22 per cent. w/v, this figure being obtained by agitating for 24 hours, solutions initially under- and super-saturated and determining the concentration of gentisic acid potentiometrically. Commercial material may be over 1·5 times more soluble than the recrystallised form. The values $pK_1 = 3{\cdot}1$ (ionisation of the carboxyl group) and $pK_2 = 10{\cdot}2$ (ionisation of the phenolic group) were determined by potentiometric titration. In the range, *p*H 5·0 to 8·0, the gentisate ion is the only component, with absorption maximum at 320 mμ. Bathochromic shift occurs below *p*H 5·0 and reproducible measurements are not possible above *p*H 8·0. The molar extinction coefficient for the acid is 4000. Gentisic acid gives a green colour with molybdophosphotungstate test solution. Since salicylic acid and other phenolic substances give this reaction only in alkaline solution, the colour in acid solution can be used for the quantitative determination of gentisic acid in the presence of salicylates. The colour measurements should be made at 670 mμ. G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Gastric Antacids, Comparative Buffering Capacities of. E. R. Hammarlund and L. W. Rising. (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41**, 295.) The maximum recommended dose of the powder or powdered tablets was added to 25 ml. of 0·1N hydrochloric acid, and stirred continuously, the *p*H being recorded every 5 minutes for the first 30 minutes. To simulate gastric secretion, 25 ml. of 0·1N hydrochloric acid was added every 30 minutes, the *p*H being read just before adding the acid, up to 3 hours. Liquid preparations were treated similarly, using 8 ml. The following of the newer preparations were tested; mixtures of aluminium hydroxide and magnesium trisilicate with and without methylcellulose, aluminium hydroxide gel with magnesium trisilicate, polamine resin, polamine resin with gastric mucin, glycine with calcium carbonate, sodium carboxymethylcellulose and milk preparations. Glycine with calcium carbonate produced the greatest rise in *p*H. Resin products used in these experiments did not raise the *p*H as rapidly as those studied previously, and sodium carboxymethylcellulose showed no chemical advantage over other types. G. B.

Insulin, Molecular Weight of. E. J. Harfenist and L. C. Craig. (*J. Amer. chem. Soc.*, 1952, **74**, 3087.) A sample of insulin which had been well characterised by countercurrent distribution and known to contain 90 per cent. or more of the A component was examined. The method of partial substitution by 1-fluoro-2: 4-dinitrobenzene, separation of the reaction products and colorimetric analysis of the monosubstituted derivative for the dinitrophenyl group

was used for the determination of the molecular weight. A molecular weight of 6500 was obtained. A. H. B.

Insulin Samples, Glycogenolytic Factor in. G. Audy and M. Kerly. (*Biochem. J.*, 1952, **52**, 70.) Assays of glycogenolytic factor content were carried out on available insulin samples as prepared by different manufacturers and on different samples from the same firm. The activity was estimated from the increased rate of production of glucose by liver slices, incubated in buffered saline, caused by the addition of the factor. The experimental procedure is described fully since satisfactory results were only obtained when all details were observed. Two methods of assay were used, the first, or single-dose method giving an approximate estimate of activity after testing at one concentration, and the second or multiple-dose method which necessitated testing of samples at several concentrations and gave a more accurate assessment of relative potency. 23 commercial insulin samples were examined and the glycogenolytic factor content was found to vary considerably although no samples had an activity greater than the sample used as a standard; several were free from glycogenolytic factor. R. E. S.

Nisin. J. L. Gowans, N. Smith and H. W. Florey. (*Brit. J. Pharmacol.*, 1952, **7**, 438.) Nisin, a relatively insoluble antibacterial substance obtained from the culture fluid of a strain of streptococcus (group N), has been found to powerfully inhibit the growth *in vitro* of many strains of *Str. pyogenes* and *Staph. aureus*, but to be much less active against *Myco. tuberculosis* than previously reported. *B. coli*, *Salm. typhi*, *Sh. shigae*, *N. meningitidis* and *N. catarrhalis* were insensitive to nisin. The activity was not destroyed by incubation with serum and tissue slices, but homogenised tissues destroyed three-fourths of the activity. Administration of a fine suspension of nisin by injection to mice and rabbits showed it not to be unduly toxic. Excretion tests showed that nisin was partly excreted by the kidney for some hours after injection. *In vivo* tests showed nisin to be ineffective against infection with a bovine strain of *Myco. tuberculosis* in rabbits, but it was effective in mice against *Str. pyogenes* and *Staph. aureus*. G. F. S.

BIOCHEMICAL ANALYSIS

Blood, Chromatographic Amino-acid Analysis of. K. V. Giri, K. Krishnamurthy and T. A. Venkitasubramanian. (*Lancet*, 1952, **263**, 562.) A technique of circular filter paper chromatography has been developed. Blood is pipetted into three times its volume of absolute ethanol and after centrifugation the protein-free ethanolic extract is mixed with three times its volume of chloroform, leaving an aqueous layer at the top of the chloroform-ethanol mixture; this aqueous solution is used for spotting on the paper in 50 μl. quantities according to the method of Giri and Rao (*Nature, Lond.*, 1952, **168**, 923). Most of the amino-acids in blood can be identified, except threonine, serine, and methionine, which always overlap the bands of glutamic acid, glycine and valine respectively; threonine and serine can be identified by treating the paper with periodate and running the chromatogram, the intensities of the glutamic acid-threonine and glycine-serine bands being decreased. The amino-acids leucine, methionine, valine, alanine, lysine, histidine, tyrosine, glutamic acid, threonine, glycine, arginine, cystine, serine, and glutamine were identified in normal blood. R. E. S.

Progesterone in Body Fluids. D. G. Edgar. (*Nature, Lond.*, 1952, **170,** 543.) Results are given for the determination of progesterone in biological material by a method based on the technique of extraction and partition between organic solvents followed by separation and semi-quantitative estimation by paper chromatography. Blood from the ovarian vein of ewes contained progesterone from 0·5 to 2 μg. per ml.; progesterone was not found in the peripheral blood. Residues left after extraction of the hormone were analysed for "bound" or conjugated progesterone and this did not exceed 15 per cent. of the total. Blood withdrawn from the caudal vena cava of a doe 25 minutes after an injection of 25 mg. of pure progesterone (in oil) showed a content of 0·2 μg./ml. Progesterone could not be detected in rabbit blood 3 hours and 8 hours after injection. Results are given for the progesterone content of cow's follicular fluid (3 μg./ml.), of ovarian cysts of sows (1 to 5 μg./ml.), and of preserved luteal tissues from an elephant ovary (2 μg./g.). R. E. S.

Steroids, Colour Reactions with Perchloric Acid. H. Tauber. (*Analyt. Chem.*, 1952, **24,** 1494.) A chloroform solution of the steroid under test is shaken with perchloric acid and heated at 56° C. for 10 minutes; distilled water is then added and the tubes reheated, the colours being observed at all stages of the treatment. Colours are recorded for cholesterol, testosterone, methyl testosterone, testosterone propionate, testosterone *cyclo*pentylpropionate, dehydro*iso*androsterone acetate, progesterone, pregnenolone, 11-desoxycorticosterone, 17-hydroxycorticosterone 21-acetate, cortisone (alcohol), œstrone, œstradiol, œstriol, œstriol benzoate, vitamin D_3 (crystalline), diethylstilboestrol, indol, skatol, catechol, resorcinol, pyrogallol, ergosterol, cholic acid. The test shows colour differences even between closely related compounds. R. E. S.

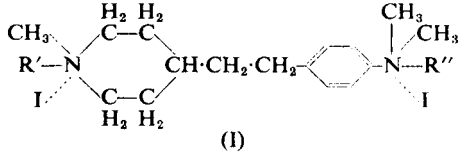
CHEMOTHERAPY

Acetoacetamides, Substituted, as Sedative Agents. R. A. LaForge, C. E. Cosgrove, R. B. Keller and U. E. Johnsen. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41,** 303.) α-Methyl, dimethyl, ethyl, propyl and *iso*propyl acetoacetamides were prepared by ammonolysis of the corresponding α-alkylacetoacetic esters. α,α-Dialkylacetoacetamides, or α-alkyl and α,α-dialkyl acetoacet-*p*-phenetidides were prepared by the reaction of α-alkylacetoacetamides or acetoacet-*p*-phenetidides with alkyl iodides. α,α-Diethyl, dipropyl, allylethyl and *iso*valeryl acetoacetamides and ethyl, propyl, dipropyl acetoacet-*p*-phenetidides were made in this way. 1-Phenyl-3-(α-alkyl or α,α-dialkylacetoacetyl) ureas were obtained by reaction of phenyl *iso*cyanate with the α-alkyl or α,α-dialkyl acetoacetamides. The methyl, dimethyl, diethyl and dipropyl members of the series were prepared. α-Chloro derivatives were prepared by the reaction of sulphuryl chloride on α-alkylacetoacetamides and α-alkylacetoacet-*p*-phenetidides. The following were sedative in a dose of 500 mg./kg. in rabbits: α-methylacetoacetamide, dipropylacetoacetamide and *iso*propylacetoacetamide. Introduction of a β-acetyl group into aliphatic amides possessing sedative properties did not enhance the sedative effect. G. B.

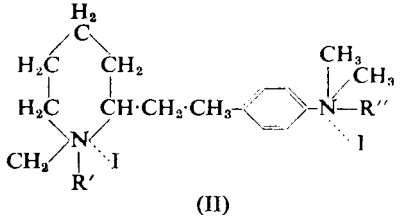
Piperazines, *N*-Substituted, as possible Sedative Agents. R. B. Keller and R. A. LaForge. (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41,** 301.) 1-*iso*Valeryl-4-methylpiperazine hydrochloride (1) was prepared by the reaction of 1-methylpiperazine with *iso*valeryl chloride when heated in dry chloroform under a reflux condenser. 1-*iso*Valeryl-4-carbethoxypiperazine (2) was prepared similarly from 1-carbethoxypiperazine. *iso*Valeryl *iso*cyanate, heated

under a reflux condenser with 1-methylpiperazine and 1-carbethoxypiperazine in dry ether yielded the corresponding *iso*valerylureas (3), (4). Reaction of nitrourea with 1-carbethoxypiperazine produced 1-carbethoxypiperazine-4-carboxamide (5). This compound yielded the corresponding *iso*valeryl biuret (6) by reaction with *iso*valeryl *iso*cyanate. Compounds (1) to (6), tested in rabbits, were not effective sedative agents. G. B.

Stilbazoline Bis-quaternary Ammonium Derivatives as Curare Substitutes. A. P. Phillips. (*J. Amer. chem. Soc.*, 1952, **74**, 3683.) Because of the powerful curare-like and related activities in certain 4- and 2-stilbazoline quaternary ammonium salts such as I and II, the structures of the alkyl groups attached



(I)



(II)

to the nitrogen atoms was varied systematically, and the relationship between structure and curare-like activity was examined. In the 4-stilbazolines the nature of the alkyl groups is critical and the completely methylated compound (I) (where $R' = R'' = CH_3$) represents maximum activity. The replacement of one methyl group from each nitrogen atom by ethyl or higher alkyl groups gave products devoid of curare-like activity. The replacement of one methyl group by ethyl at either nitrogen atom gave a reduction in activity. In the 2-stilbazolines (II), increasing the alkyl group size does not diminish the antagonistic action which these compounds have in reversing the myoneural block of (I) (where $R' = R'' = CH_3$). A. H. B.

PHARMACY

GALENICAL PHARMACY

Disintegrating and Binding Agents in Compressed Tablets, A Statistical Study of. E. A. Holstius and H. G. DeKay. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 505.) Tablets containing sulphathiazole, sodium bicarbonate and aspirin compound, representing 3 different types of tablet were prepared according to the same formula, 324·6 mg. of active constituent being used with 38·9 mg. of lactose as filler, 38·9 mg. of disintegrating agent, 3·9 mg. of lubricant and a sufficient quantity of binder. All tablets were prepared in a small single-punch machine using a $\frac{3}{8}$ inch die and standard concave stainless steel punches. Hardness was maintained at 4·0 kg./cm.^{2} (Monsanto hardness tester). Arrowroot, maize, potato, sweet potato, rice, sorghum, tapioca and wheat starches were investigated as disintegrating agents, and gelatin-acacia solution, sucrose solution and starch paste were used as binders. Disintegration times were

determined and submitted to a 3-way statistical analysis to ascertain what factors significantly affected the rate of disintegration. Of the variables investigated (active constituent, binding agent, and disintegrating agent) it appears that none is solely responsible for determining the disintegration rate of the finished tablet, which is probably due to an interaction of the three main effects. Thus there is no universal disintegrating agent which would provide the same rate of disintegration in all tablets. G. B.

NOTES AND FORMULÆ

Meralluride (Mercuhydrin) Suppositories. (*New and Nonoffical Remedies, J. Amer. med. Ass.*, 1952, **149**, 442.) Meralluride, a mixture of 1-(3′-hydroxymercuri-2′-methoxypropyl)-3-succinylurea and theophylline, is a mercurial diuretic official in the U.S.P. Mixed with sodium bicarbonate, it is used in the form of suppositories as a supplement to parenteral administration. The following tests are described for the suppositories. When refluxed with formic acid, a grey precipitate of mercury is deposited. The supernatant liquid, when cooled in ice, yields a precipitate of allylsuccinylurea, which melts at 145° to 148° C. When the remaining liquid is freed from residual mercury with hydrogen sulphide, treated with sodium acetate, and extracted with chloroform, it yields, on evaporation of the chloroform, a residue of theophylline. The suppositories should contain 90·0 to 110·0 per cent. of the labelled amount of mercury and of anhydrous theophylline. The content of mercury is determined by heating with a very dilute solution of sodium hydroxide until the material is dissolved, refluxing with nitric acid and titrating with ammonium thiocyanate. The theophylline is determined by heating with a dilute solution of ammonia until the material is dissolved, adding silver nitrate, and estimating the precipitate thus obtained by dissolution in nitric acid and titration with ammonium thiocyanate. G. R. K.

PHARMACOGNOSY

Digitalis Extraction Studies. G. G. Krishnamurty and O. Gisvold. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 152.) Glycosides obtained from fresh leaves of *Digitalis lanata* by Stoll's enzyme inhibiting techniques appeared to be identical with those obtained by extracting the fast-frozen and powdered fresh leaves as described in the previous paper. Plants raised from Swiss seed yielded material identical with that from the Minnesota plants. When fresh disintegrated leaves were incubated at 40° C. for 8 hours before extraction there was a slight decrease in glycosidal yield. After 24 hours' incubation there was a lower yield and leaves incubated for 48 hours yielded no crystalline glycosides on extraction. Leaves which had been stored for 1 year under damp conditions gave no crystalline glycosidal material, but carefully dried and powdered leaves gave a yield similar to that of the fresh leaves. G. B.

PHARMACOLOGY AND THERAPEUTICS

Amodiaquin (Camoquin), Superiority over Other Antimalarials. I. Singh and T. S. Kalyanum. (*Brit. med. J.*, 1952, **2**, 312.) Clinical trials were carried out in soldiers who had contracted tertian malarias. Amodiaquin and chloroquin were superior to proguanil, mepacrine and combinations of proguanil with mepacrine or quinine. In benign tertian malarias, the average duration of fever was 24 hours with amodiaquin and 36 hours with chloroquin, the average

time for clearance of parasitæmia being 40 and 38 hours respectively. In malignant tertian malarias, the average duration of fever in amodiaquin treatment was halved compared with chloroquin, parasitæmia being cleared in an average of 33 and 48 hours respectively. With larger doses of amodiaquin, relapses were few and delayed. A further advantage was that the cost was lower and only a single dose was required. G. B.

Belladonna, Action of, on Gastric Motility in Man. W. F. Anderson. (*Lancet*, 1952, **263**, 255.) Experiments were performed in 29 normal subjects, 2 with duodenal ulcers and 1 with ulcerative colitis, contractions of the stomach being recorded by Carlson's balloon method. Small doses (up to 30 minims) of tincture of belladonna administered by mouth slowed the pulse rate and increased the frequency and amplitude of active gastric contractions. With larger doses, the initial parasympathomimetic phase was followed by an increase in the pulse rate and cessation of gastric contractions. Atropine sulphate by mouth or parenterally produced the same effects, but rather more slowly than belladonna. The administration of atropine sulphate in a solution containing the same concentration of ethanol as tincture of belladonna had no effect on the speed of action. G. B.

Cortisone and Salicylate, Antagonistic Effects of. M. J. H. Smith. (*Nature, Lond.*, 1952, **170**, 240.) In experiments on adrenalectomised rats, salicylate in the presence of cortisone caused a significant depletion of liver glycogen at 6 hours, whereas cortisone alone caused a significant deposition. Sodium salicylate reduced the glycosuria produced by cortisone in normal rats and also reduced the hyperglycæmia after feeding. It has been suggested that salicylates act through the pituitary and adrenal cortex, producing adrenal corticoids. The results do not agree with this theory, according to which cortisone and salicylates should have a similar effect. G. B.

Cyanocobalamin (Vitamin B_{12}) and Liver Extract in Maintenance Treatment of Pernicious Anæmia, Comparison of. E. K. Blackburn, J. Burke, C. Roseman and E. J. Wayne. (*Brit. med. J.*, 1952, **2**, 245.) The authors report the results of treating 60 pernicious anæmia patients for lengthy periods with injections of cyanocobalamin (vitamin B_{12}). A group of 22 of these patients had previously received prolonged treatment with injections of liver extract and were observed for at least 2 years while receiving injections of cyanocobalamin, the dose varying from 40 to 160 μg. per month. Two further groups, each of 10 patients, had received either liver extract alone or cyanocobalamin alone since the onset of their illness. The initial dose of cyanocobalamin for the patients previously on liver extract was 10 μg. for each ml. of liver extract previously found necessary; the remainder responded similarly to treatment but the periods of observation were shorter. Blood counts and clinical examinations were carried out on all the patients at intervals of 6 to 8 weeks. Statistical examination of the results in the first group of 22 patients showed that vitamin B_{12} gives a significantly better result than liver extract. In the two groups of 10, those previously receiving cyanocobalamin alone had significantly higher red-cell counts and hæmoglobin concentrations than those receiving liver extract alone. All the patients were maintained in good health and a few were strikingly better on cyanocobalamin than on liver extract. One patient relapsed because of too infrequent dosage. No evidence was found of sore tongue, gastro-intestinal disturbance, neurological involvement or leucopenia. Injections of cyanocobalamin solution have the advantages that

they are small in bulk, constant in potency, relatively cheap and do not lead to sensitisation. For patients without neurological involvement a maintenance dose of at least 50 μg. a fortnight is recommended. H. T. B.

Decamethonium-like Agents: Conversion to Tensilon-reversible Agents by Aromatic Substituents. L. O. Randall. (*J. Pharmacol.*, 1952, **105**, 16.) 5 analogues of decamethonium containing nitrobenzyl radicals in place of methyl groups on the nitrogen atoms were found to resemble *d*-tubocurarine in being reversible by 3-hydroxyphenyldimethylethylammonium chloride (tensilon). Maximal potency in cats was reached in compound Ro 2-4501, *N,N'*-nonamethylenebis-[dimethyl-(*p*-nitrobenzyl) ammonium bromide] dihydrate. It was less active than *d*-tubocurarine on sympathetic ganglia and blood pressure, but equally active on the vagus endings. The nitrobenzyl and cyanobenzyl analogues of mytolon chloride were also tensilon-reversible. The nitrobenzyl compounds, Ro 2-4395, *N,N'*-(2:5-dihydro-2:5-dioxo-1:4-phenylene)bis-[3-aminopropyl-(*p*-nitrobenzyl)-diethylammonium chloride] dihydrate, was more active than *d*-tubocurarine in the cat and rabbit, equally active in the mouse and pigeon, and less active in the monkey; it had lower ganglionic blocking action and blood pressure effects but equal vagal blocking action. 8 analogues of succinylcholine, dipropamine and similar agents containing the nitrobenzyl radical instead of alkyl groups on the nitrogen atoms were tensilon-reversible. The most active compound, Ro 2-4658, γ,γ'-(*p*-phenylenedioxy)bis-[diethyl-(*p*-nitrobenzyl)-propylammonium bromide] dihydrate, was stronger than *d*-tubocurarine in the cat, mouse, and rabbit, equal in the pigeon, but weaker in the monkey; the ganglionic blocking action and blood pressure effects were weaker, but the vagal blocking action stronger. The nitrobenzyl group when substituted for alkyl groups on the nitrogen atoms of bis-quaternary ammonium compounds appears to have the property of converting tensilon-irreversible agents of the *d*-tubocurarine type. S. L. W.

Isoniazid in Treatment of Tuberculous Meningitis in Children. W. P. Sweetnam and E. F. Murphy. (*Lancet*, 1952, **263**, 160). 4 children with tuberculous meningitis were treated with isoniazid orally, 2 receiving the drug for 8 and 9 weeks respectively and 2 for 10 weeks. 3 of the patients were given streptomycin either initially or concurrently. After treatment with streptomycin was thought to be producing deafness, the first patient was given 4 mg. of isoniazid per kg. of body weight daily in 6-hourly doses, increased after 2 days to 8 mg./kg., and after 8 weeks to 16 mg./kg. Improvement in the cerebrospinal fluid did not occur until this dose was given but intolerance characterised by vomiting and diarrhœa occurred and treatment had to be stopped after a further week, although the clinical improvement continued. The second patient was given isoniazid in addition to streptomycin after failing to respond to streptomycin alone. The dose of isoniazid was 4 mg./kg. per day increasing to 8 mg./kg. after 2 days. After a further 2 days marked improvement was apparent. The third patient showed an initial response to streptomycin and to isoniazid but a later deterioration was not influenced by the two drugs given concurrently. The fourth patient gave a dramatic response after only 3 days on isoniazid, 8 mg./kg., alone. Treatment was continued for 8 weeks but was then stopped because the patient developed mild infective hepatitis. Except for the signs of intolerance on the dose of 16 mg./kg. there were no signs of drug toxicity other than a temporary fall in hæmoglobin level which was reversible without stopping treatment. H. T. B.

Metallic Salts, Irritant Action of, on Intestinal Mucosa. A. L. Picchioni and L. D. Edwards. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 289.) A white rat was fasted and then given food 1 hour prior to being killed. A segment of its intestine was placed in a bath of Ringer-Locke solution at 38° C. with aeration and arrangements for filling and emptying the lumen and recording contractions. After 30 minutes, nutrient fluid was introduced into the lumen and normal contractions recorded. The process was repeated with Ringer-Locke solution without bicarbonate and glucose, to which a heavy metal salt was added. The minimum concentration of the irritant required to produce the characteristic pattern of intense, disorganised irreversible contractions was determined in several experiments of this kind. Low concentrations of zinc, copper and mercury salts, and of iron salts which give solutions of low *p*H, modified peristalsis. Aluminium salts, ferric ammonium citrate, ferric glycerophosphate and ferric tartrate showed the least effect. A *p*H less than 2·0 or more than 11·0 was found to be irritant. G. B.

***iso*Nicotinyl Hydrazide.** P. Klee. (*Dtsch. med. Wschr.*, 1952, **77**, 578.) Unlike other new antituberculosis drugs, *iso*nicotinyl hydrazide has no undesirable side effects, and produces an increase in appetite and a subjective feeling of well-being. The optimal dose was found to be, for a mean body weight of 50 to 60 kg., 0·5 to 0·9 g./day, taken in 4 doses after meals. Since animal experiments have indicated a possibility of cumulation, after 10 days the drug is discontinued for a few days, although this does not appear to be essential. For parenteral use a 2 per cent. solution, which is isotonic, is satisfactory; while for intralumbal application in tubercular meningitis 1 to 2·5 ml. of the same solution may be diluted with 10 ml. of liquor. The latter form of application has only been tested on adults. Actually higher doses have been administered without harm, e.g., 1·35 g. in a single dose, and 91·6 g. in 130 days. Biological tests show that the sera of patients receiving such doses is able to prevent the growth of streptomycin-resistant strains of *Myco. tuberculosis*. The results of treatment were evaluated on 61 patients, of which two-thirds showed rapid improvement, while none became worse. Increase of appetite, followed by increase in weight, was general. Some patients who had only become worse when treated with streptomycin, *p*-aminosalicylic acid and thiosemicarbazones, showed considerable improvement with *iso*nicotinyl hydrazide. G. M.

Phenylbutazone in Rheumatoid Arthritis and Gout. W. C. Kuzell, R. W. Schaffarzick, B. Brown and E. A. Mankle. (*J. Amer. med. Ass.*, 1952, **149**, 729.) Phenylbutazone (Butazolidin) is the sodium derivative of 4-butyl-1:2-diphenyl-3:5-pyrazolidinedione and has been widely used in conjunction with amidopyrine because it increases its solubility and makes it possible to give amidopyrine by injection. The combination has a marked antirheumatic action and for this reason the authors investigated the effect of phenylbutazone alone in gout and various rheumatic diseases. The compound was given in the form of tablets containing 0·125 or 0·2 g. in doses of 1 to 6 tablets per day or as intramuscular injections of a 20 per cent. solution in single daily doses of 0·6 to 1 g. All of 48 patients with gout showed clinical improvement; of 19 who had previously been given colchicine, 9 responded better to phenylbutazone and 3 responded better to colchicine. Comparison was made in 20 patients of the effects of phenylbutazone alone and of a phenylbutazone and amidopyrine combination; equal improvement was shown in 13 while phenylbutazone alone was better in 4. Effects in rheumatoid arthritis were

evaluated according to the criteria of the American Rheumatism Association. 21 out of 29 patients showed grade I or grade II response and all showed some improvement. Administration had to be continued and there was no improvement in the erythrocyte sedimentation rate. Some improvement occurred in ankylosing spondylitis and osteoarthritis and also in postmenopausal osteoporosis of the spine, in which condition sex hormone therapy was given concurrently. Toxic manifestations included skin rashes, œdema, nausea, activation of peptic ulcer, and pain at the site of injections; they occurred in 47 out of 140 patients treated but were sufficiently severe to necessitate discontinuing the treatment in only 17. The compound does not affect the adrenal ascorbic acid content, thus suggesting that it does not act by stimulating the adrenal cortex directly, nor does it produce changes in the blood picture.

H. T. B.

Procaine Amide Hydrochloride, Pharmacology of. G. Manchetti. (*Arch. ital. Sci. Farmacol.*, 1952, **2**, 134.) Procaine amide hydrochloride is the hydrochloride of *p*-amino-*N*,2-diethyl-4-amino(2-diethylaminoethyl) benzamide. It is an ivory-white powder, very soluble in water, soluble in ethanol (95 per cent.), insoluble in ether, m.pt. 167° to 168° C. The minimum lethal dose for rabbits is 0·25 g./kg. by slow intravenous injection, 0·75 g./kg. for intramuscular injection and 1·5 g./kg. by the mouth; 1 g./kg. was well supported. It has a strong antifibrillary action. When 0·02 mg./kg. of adrenaline is injected into dogs they invariably die from ventricular fibrillation, the simultaneous injection of from 20 mg. to 100 mg./kg. of procaine amide enables 60 per cent. to survive. Procaine is rapidly hydrolysed by human blood serum, little being left after an hour; 90 per cent. of procaine amide is present after 24 hours. It reduces blood pressure, in doses of 30 to 50 mg./kg., by 20 mm. of mercury in the dog and 20 to 50 mm. in the rabbit, but recovery is rapid. It is rapidly absorbed from the intestine of the rat and elimination, which is by the kidneys, is slow, about half being excreted unaltered in 24 hours, 70 to 90 per cent. is excreted in 48 hours, during the latter period it is partly excreted as *p*-aminobenzoic acid. Similar results were obtained in man. Thus procaine amide has a low toxicity and considerable antifibrillary action; it is readily absorbed, stable in the blood and slowly excreted.

H. D.

Sulphones and Streptomycin in Pulmonary Tuberculosis. P. W. Edwards, A. C. Penman and L. J. Cutbill. (*Brit. med. J.*, 1952, **1**, 1224.) 22 patients received combined treatment with diaminodiphenylsulphone and streptomycin. The aim of the trial was to determine if the sulphone prevented or delayed the emergence of streptomycin-resistant strains of the tubercle bacillus, and to compare the results with a similar series treated with streptomycin and *p*-aminosalicylic acid. 50 mg. of the sulphone was given twice daily for the first 2 weeks; from the 3rd week 1 g. of streptomycin was given daily by intramuscular injection and the sulphone dosage was increased to 100 mg. twice daily, and after another 2 weeks to 100 mg. thrice daily. The intention was to give streptomycin for a minimum of 8 weeks and the sulphone for a minimum of 12 weeks, but after the appearance of hæmolytic anæmia in 3 cases sulphone treatment was suspended. The dosage was then reduced to 25 mg. daily increasing to 50 mg. daily after 2 weeks, and thereafter blood changes were not alarming. In 15 out of the 22 cases the organism was isolated from the sputum and tested for streptomycin sensitivity before treatment was started; 11 strains were fully sensitive, and 4 showed some reduction in sensitivity; the remaining 7 cases were negative. 12 strains were isolated either during treatment or after its

completion. Of these, 1 was fully sensitive, 3 showed reduced sensitivity, and 8 were completely resistant to streptomycin. Because of the rapid emergence of resistant strains the trial was stopped after it had been made in 22 cases. These results were not encouraging and compared very unfavourably with the findings in the streptomycin and *p*-aminosalicylic acid group of the M.R.C. (1950). The trials also demonstrated that diaminodiphenylsulphone in doses of 200 mg. daily is not tolerated by European tuberculous patients. S. L. W.

Synthetic Curare-like Agents Reversible by 3-Hydroxyphenyldimethylethylammonium chloride (Tensilon). L. O. Randall. (*J. Pharmacol.*, 1952, **105**, 7.) A series of 27 bis-quaternary bipiperidine derivatives were assayed for curare-like activity. The replacement of alkyl radicals on the nitrogen atoms by aromatic radicals converted tensilon-irreversible agents of the decamethonium type to tensilon-reversible agents of the tubocurarine type. The highest potency was reached in compound Ro 2-4377, 4,4′-ethylenebis-[1-(*p*-nitrophenethyl)-1-methylpiperidinium bromide]. Besides being antagonised by tensilon, Ro 2-4377 had relatively weak blood pressure effects and ganglionic blocking action, but relatively strong vagolytic action. In the nitrobenzyl substituted series, maximal potency in cats was reached in compound Ro 2-3799, 4:4′-ethylenebis-[1-(*p*-nitrobenzyl)-1-methylpiperidinium bromide], which also has 8 carbon atoms between the nitrogen atoms. The compounds having various substituents on the nitrogen atoms had a decreasing order of potency as follows: nitrophenethyl, nitrobenzyl, cyanobenzyl, carbamylbenzyl, acetylbenzyl, phenethyl, carbethoxybenzyl, methylsulphonylbenzyl, methylmercaptobenzyl, benzyl, and phenyl propyl. S. L. W.

***Veratrum viride*, Bioassay of.** H. J. Jenkins and B. V. Christensen. (*J. Amer. pharm. Ass., Sci. Ed.*, 1952, **41**, 239.) A 1 in 10 dilution of each of two tinctures of veratrum, U.S. National Formulary VII was injected into the brachial veins of pigeons and the median emetic dose (M.Em.D.50) determined. Doses of the 1 in 10 dilutions of the tinctures were administered to dogs anæsthetised with pentobarbitone sodium and the maximum blood pressure reduction corresponding to each dose was measured. The M.Em.D.50 dose was also administered to human patients with essential hypertension and the maximum blood pressure reduction observed. The pigeon emetic test gives a sharply reproducible end-point. Since a quantitative relationship exists between pigeon emetic dose and blood pressure response in dogs and the same relationship may be demonstrated in human patients as in dogs, the pigeon emetic test may be used to measure the therapeutic effects of *Veratrum viride*. G. B.

Vitamin B_{12} (Cyanocobalamin), Maintenance Therapy of Pernicious Anæmia with. D. A. Brewerton and R. A. J. Asher. (*Lancet*, 1952, **263**, 265.) A study was made with 36 patients previously treated with injections of liver for at least 1 year and subsequently treated with a preparation of cyanocobalamin for more than 20 months. On average, 1 liver injection was required every 19 or 1 cyanocobalamin injection every 25 days. Generally patients preferred the cyanocobalamin treatment. It caused no untoward reactions, whereas 36 per cent. of patients had unpleasant reactions during treatment with liver injections. No neurological complications developed during vitamin B_{12} therapy, which has the advantage that its potency is reliable and that treatment is cheaper than with the proprietary liver injections. G. B.

Vitamin K, Effect of, on Hypoprothrombinæmia Induced by Dicoumarol and Tromexan. A. S. Douglas and A. Brown. (*Brit. med. J.*, 1952, **1**, 412.) A

test dose of dicoumarol or tromexan was given to human patients and prothrombin levels determined at least daily. After the prothrombin time had returned to normal, the same dose of the anticoagulant was given together with a dose of a vitamin K preparation, and the prothrombin levels were again determined. Vitamin K_1 given intravenously in doses of 200 to 340 mg. blocked completely the action of the anticoagulants and restored the prothrombin to a safe level within a few hours, even when the hypoprothrombinæmia had been greater than is usually necessary for therapy. Menaphthone and kapilon (2-methyl-1 :4-naphthohydroquinone carboxymethoxine) by intramuscular injection, acetomenaphthone orally and synkayvite (2-methyl-1 :4-naphthohydroquinone diphosphate) and water-soluble K analogue (dipotassium 2-methyl-1 :4-naphthylene bisulphate) by intravenous injection were all relatively ineffective against the hypoprothrombinæmic effect. For intravenous infusion, the suspension of vitamin K_1 was prepared as follows. Dissolve 200 mg. in 4 ml. of ethanol and mix with 5 per cent. glucose solution to produce 250 to 500 ml. Suspension of the vitamin is assisted by injecting the ethanolic solution through a long fine needle into the glucose solution. Autoclave and use immediately as the product is unstable. G. B.

BACTERIOLOGY AND CLINICAL TESTS

Antibiotics, Sensitivity of *Staphylococcus pyogenes* to. M. A. Birnstingl, R. A. Shooter and M. F. Hunt. (*Brit. med. J.*, 1952, **2**, 253.) Because of cross-infection in hospitals, figures for the incidence of resistance to antibiotics amongst strains of *Staphylococcus pyogenes* isolated from in-patients do not give a fair indication of the incidence of resistance amongst the general population. The authors have therefore determined the incidence of resistance amongst strains isolated from out-patients with staphylococcal skin infections, all staphylococci which coagulated plasma in a tube being described as *Staph. pyogenes*. Each strain was tested against penicillin, streptomycin, aureomycin, chloramphenicol and terramycin. In each case a large inoculum was used. Against penicillin, 16 per cent. of the strains were resistant, compared with 6·5 per cent. in the same hospital three years earlier. Against the other antibiotics, none of the strains was resistant but the usual minimum inhibitory concentration of chloramphenicol was 32 times that of aureomycin and 16 times that of terramycin. H. T. B.

Sterility Tests of Solutions for Parenteral Administration. P. N. Sen Gupta. (*Ind. J. med. Res.*, 1952, **40**, 115.) The bacteriostatic activity of some 85 commonly used chemical solutions for parenteral administration was tested against *Staph. aureus*, *Ps. pyocyaneus* and *B. subtilis*. A papain digest meat broth medium was employed and the tubes were inoculated with an 18-hour broth culture of the different organisms. The tubes were incubated for 24 hours at 37° C. and those showing free growth similar to that in the control tubes were taken to have been sufficiently diluted so as not to interfere with free growth of the contaminants. The lowest dilution employed of the parenteral solutions was 1 in 10 (i.e., dilutions of the solutions in the strengths commonly employed, not of the chemicals present in them). Of the 85 solutions 60 showed no bacteriostatic action in dilutions of 1 in 10; the remainder showed bacteriostatic action against one or more of the test organisms in dilutions of 1 in 10 or upwards. In this latter group the approximate volume of medium to be used in each case for the sterility test is indicated. S. L. W.