tinned foods, and relying as much as possible on a diet made up of fruits, sugar, boiled rice, and fresh vegetables.

A simple diuretic such as hydrochlorothiazide 50 mg. b.d. should be supplemented in resistant cases with spironolactone 25 mg. four times daily; potassium supplements such as potassium chloride 15 g. t.d.s. are usually required to prevent hypokalaemia. In addition to the measures mentioned above, digoxin may be required in cardiac disease.

In the nephrotic syndrome steroids are sometimes effective. A high protein diet—100 g. of protein a day—is required in malnutrition, nephrotic syndrome (without azotaemia), and in hepatic cirrhosis (provided signs of hepatic precoma are absent). Vitamin supplements are also useful in malnutrition and states of suspected undernutrition. Alcohol is forbidden in all patients with hepatic cirrhosis.

Paracentesis

The removal of ascitic fluid is often required for diagnostic purposes and for the relief of discomfort in patients with massive ascites. Because of serious complications like hypotension, oliguria, hyponatraemia, and hepatic coma, which have sometimes followed massive evacuation of ascitic fluid, it is wise to limit the fluid removed on each occasion to 2–3 l.

Malignant Ascites

The treatment of ascites due to malignant disease is usually unrewarding, but in the lymphomas, including Burkitt's tumour, chemotherapy with nitrogen mustards and related agents may occasionally produce surprising results and should be given a trial wherever feasible.

The drug used most often in these cases is cyclophosphamide, which is given intravenously in doses of 30–40 mg./kg. body weight.[13] One or two doses are often adequate to produce remissions lasting from months to several years in responsive cases of Burkitt's tumours. These drugs are marrow depressants, and should be used only by those who are familiar with their side-effects.

I wish to express my gratitude to Professor J. C. Edozien, of the Department of Chemical Pathology, for the ascitic fluid protein determinations.

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TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

New Drugs against Tuberculosis

Capreomycin and ethambutol are new antituberculosis drugs undergoing clinical trial. They are the subject of a recent monograph published by the New York Academy of Science.[1]

Capreomycin

Capreomycin is a peptide antibiotic derived from *Streptomyces capreolus*. There is no cross-resistance with streptomycin but there are varying degrees of cross-resistance with viomycin and kanamycin. Patients who have received previous treatment with either of these drugs may have organisms resistant to capreomycin.

The toxicity of capreomycin is similar in type to that of streptomycin. In the usually recommended dose of 1 g. daily vestibular disturbance, deafness, and renal impairment have occurred. The incidence of ototoxicity appears to be no greater than that with streptomycin. The reported incidence of nephrotoxicity has varied, and more needs to be known about its long-term effects. Regular observations of renal function should be maintained during capreomycin therapy.

Used as the only companion drug to either P.A.S. or isoniazid, capreomycin appears to be less effective than streptomycin in the treatment of pulmonary tuberculosis. Given in combination with both P.A.S. and isoniazid in a controlled trial in Japan, capreomycin was as effective as streptomycin. However, capreomycin has no place in the initial treatment of new cases of tuberculosis except to replace streptomycin in patients with intractable streptomycin hypersensitivity. The main indication for capreomycin is as a secondary drug for the treatment of drug-resistant tuberculosis. Capreomycin is less toxic than viomycin and kanamycin, and may be used in preference to these. It is of no value in treating infections other than tuberculosis. It is a relatively expensive drug.

Capreomycin is marketed under that name by Dista Products Ltd The basic N.H.S. cost of 5 vials of 1 g. is 58s. 10d.

Ethambutol

Ethambutol is a synthetic compound whose chemical structure ((+)-*NN'*-Di-(1-hydroxymethylpropyl)ethylenediamine) differs from all other antituberculosis drugs. It is active against *Mycobacterium tuberculosis, M. bovis,* and some anonymous mycobacteria but is inactive against other organisms. No cross-resistance with other antituberculosis drugs has been observed.

Studies in which ethambutol has been given as the only drug have confirmed a favourable effect in human pulmonary tuberculosis. The emergence of ethambutol-resistant organisms in many of these patients indicates the need to combine ethambutol with another drug to prevent resistance.

Controlled studies in pulmonary tuberculosis comparing ethambutol and isoniazid with P.A.S. and isoniazid have been made in Japan and the U.S.A. The results suggest that ethambutol 25 mg./kg. body weight in a single daily dose may be as effective as P.A.S. as a companion drug to isoniazid. Ethambutol has proved promising as an addition to the armamentarium of secondary drugs for the treatment of patients whose organisms are resistant to the primary drugs streptomycin, isoniazid, and P.A.S. Ethambutol in doses of up

to 50 mg./kg. body weight daily is notably free of toxic effects with the single exception of ocular toxicity. Two types of retrobulbar neuritis have occurred; one involving the central optic nerve fibres producing diminished visual acuity, central scotoma, and loss of ability to see green, and the other involving the periaxial fibres causing peripheral visual-field defect without disturbance of visual acuity or colour vision. Both eyes are usually affected. Recovery is usually complete after stopping ethambutol. The incidence of retrobulbar neuritis is dose related. Doses of 25 mg./kg. body weight or less appear to carry a small risk. Regular examination of visual acuity is necessary throughout treatment.

More information about ocular toxicity will be required before ethambutol can be accepted as a primary drug for the treatment of new cases of tuberculosis. Ethambutol has not yet been passed by the Committee on Safety of Drugs for marketing and nothing has been reported about its price.

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Toxicity of Oral Contraceptives

Q.—*Are there likely to be any ill-effects in small children who help themselves to, say, four to ten Lyndiol or other oral contraceptive tablets?*

A.—The ill-effects theoretically possible in a child who has taken a small number of oral contraceptive pills are liver toxicity, some temporary interference with the function of the seminiferous tubules, and slight withdrawal bleeding in a girl. The last two would depend on the biological half-life of the particular agent swallowed.

In terms of practical management this means that the stomach should be emptied if the tablets have been swallowed recently, and liver function should be checked by, for example, transaminase level determination two to three times in the two weeks after ingestion.

Toxicity of Methylated Compounds

Q.—*What is the pharmacological explanation of the very high toxic effect of nearly all methylated compounds—for example, methyl alcohol, methyl bromide, methyl chloride, methyl mercury compounds, etc.?*

A.—The assumption that "nearly all" methylated compounds are very toxic is not well founded. The toxicity of methyl alcohol is largely due to its metabolites formaldehyde and formic acid. These compounds would also be formed if appreciable hydrolysis of methyl bromide or chloride took place and was followed by oxidation. Combination of heavy metals with alkyl radicles produces lipoid-soluble substances which gain access to the brain more readily than inorganic metallic compounds. The difference in toxicity between methyl and ethyl metallic compounds is marginal.

In many other circumstances methyl groups have no particular adverse effect—for instance, in all the methonium compounds, or in adrenaline as compared with noradrenaline, or in methacholine, methadone, methamphetamine, methaqualone, methyltestosterone, methicillin, methohexital, and methylcellulose. Naturally the pharmacological properties are sometimes altered by the change in molecular structure, but the change is not always towards increased toxicity.

Birth Weight in Pygmies

Q.—*Is there any information on the birth weight of pygmies?*

A.—The only satisfactory study of the birth weights of pygmies seems to be that of Vincent, Jans, and Ghesquiere carried out in the late 1950's. In an important paper[1] they report various physical measurements of African (Ituri) pygmies from the Wamba area of the Congo (Leopoldville). Weights of 32 babies were recorded at a maternity clinic in the first or second day of life. The mean weight was 2,573 g. and the standard deviation 353 g. One of the babies weighed 1,500 g. and the others between 2,100 g. and 3,000 g.

In earlier literature, statistics given by Krogman[2] of birth weights of four boys and four girls (with means of 3.6 kg. and 3.9 kg.) have been quoted. The data are taken from a paper by Schebesta and Matiegka,[3] but Vincent, Jans, and Ghesquiere state[1] that the children were Bantu and not pygmies.

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Inheritance of Systemic Lupus Erythematosus

Q.—*Is there an increased risk of the development of systemic lupus erythematosus in the children of a marriage when the wife's mother died of this disease and the husband's sister suffers from it?*

A.—There is increasing evidence that a genetic factor is implicated in systemic lupus erythematosus and in the other diseases in which there also appears to be a breakdown in the mechanism regulating autoantibody formation. Systemic lupus erythematosus has more than once been reported in identical twins, and different "collagen diseases" have occurred in members of a single family.

Although the mode of inheritance is unknown, one can guess that it will prove to be multifactorial. This means, of course, that gene cumulation progressively increases the probability of developing the disease. The short answer to the question is therefore that the risk of the children developing systemic lupus erythematosus is almost certainly increased.

A recent book on lupus erythematosus[1] gives an excellent review of this problem and many references to the literature.

REFERENCE
[1] *Lupus Erythematosus*, edited by E. L. Dubois, 1966. McGraw-Hill, New York.

Mumps in Pregnancy

Q.—*Is mumps in early pregnancy known to be associated with a risk of congenital abnormality in the baby? Should gamma-globulin injections be given to pregnant women who have been exposed to infection?*

A.—There is no evidence that maternal mumps is followed by an increased risk of abnormality in the baby.[1 2] Accordingly, there are no indications for giving gamma-globulin injections to women who have been exposed to infection.

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Oral Polio Immunization

Q.—*Is there any contraindication to giving trivalent oral polio vaccine to a child aged 7 with a history of eczema following vaccination and a family history of urticaria in one sibling and death from angioneurotic oedema in another?*

A.—It can be assumed that the polioviruses in the oral (Sabin) vaccine will not provoke any abnormal reactions, but in view of the familial history of allergies there is a slight increase in the remote risk of hypersensitivity reactions to traces of materials used in the manufacture of the vaccine. Penicillin sensitivity accounted for most of these reactions in the past, but current vaccines do not contain detectable amounts of the antibiotic.

A patch test using oral polio vaccine may reveal the presence of sensitizing antibodies, but this test cannot be regarded as entirely reliable.

Correction

In the article "Relative Hypercalciuria in Nephrolithiasis," by Dr. L. C. Isaacson and his colleagues (*B.M.J.*, 1966, 2, 558), the urinary ammonium concentrations given in Table II and Table III should have been half the amount shown.