Current Practice

TODAY'S DRUGS

Food or Drug?

General practitioners may prescribe for their patients on form E.C.10 "proper and sufficient drugs and medicines and prescribed appliances."[1] Food, drink, and toilet preparations may not be prescribed. If a doctor prescribes a substance which is on the borderline between drugs and food, and the local executive council takes the view that the substance is not a drug, it will notify him that the cost of the preparation will be recovered from him unless he wishes the matter to be referred to the local medical committee. Regulation 16 of the National Health Service (Service Committees and Tribunal) Regulations, 1956, provides means of appeal to independent referees.

The Standing Joint Committee* on the Classification of Proprietary Preparations published last month[2] a report on the definition of drugs and borderline substances. The report is being sent to all doctors in the N.H.S. It is made clear in the report that the Committee does not wish and is not able to interfere with the statutory procedure, but it has set out to suggest a basis for the definition of a drug or of a food that will be acceptable to all concerned as reasonable.

Definitions

The Committee defines a drug as a "substance that has a pharmacological effect in the body, and is used to prevent or treat disease." A food is defined as a "substance that is taken to replace the physiological waste of tissue, to supply energy and heat, and to build up tissues."

Exceptions

The Committee accepts that for certain patients normal foods are unsuitable, and it gives a list (see Table) of preparations which, though usually regarded as foods, may be prescribed as a drug.

The Committee suggests that vitamin preparations should be regarded as foods when given to healthy children, factory workers, and athletes. It states that "alcoholic beverages cannot be regarded as drugs," and suggests that rectified spirit should be ordered when a spirit beverage such as gin is required in certain mixtures.

Preparations Normally Regarded as Foods, But Which Would be Regarded as Drugs When Used in the Treatment of the Diseases Shown

Product	Conditions in Which it Would be Regarded as a Drug
Aminex	Phenylketonuria and tyrosinaemia
Allergilac	Milk allergy
Casilan	Biochemically proved hypoproteinaemia
Cow and Gate L.C. Food	Intolerance to calcium
Cow and Gate L.L. Food	Fat intolerance with associated gastro-intestinal disturbances and gastroenteritis
Cow and Gate Lacidac H.C.	Fat intolerance with associated gastro-intestinal disturbances and gastroenteritis
Cow and Gate Lacidac Separated	Fat intolerance with associated gastro-intestinal disturbances and gastroenteritis
Cymogran	Phenylketonuria
Edosol	Nephritis with salt retention
Galactomin	Galactosaemia
Gluten-free flour	Gluten-sensitive enteropathies
Gluten-free Liga biscuits	Coeliac disease
Locasol	Intolerance to calcium
Lofenalac	Phenylketonuria
Minafen	Phenylketonuria
Prosol	Sprue, steatorrhea, and coeliac disease
Rite Diet gluten-free bread	Gluten-sensitive enteropathies
Rite Diet gluten-free flour	Gluten-sensitive enteropathies
Rite Diet gluten-free rusks	Gluten-sensitive enteropathies
Rite Diet protein-free bread (salted and unsalted)	Proved chronic renal failure and phenylketonuria
Rite Diet protein-free flour (salted and unsalted)	Proved chronic renal failure and phenylketonuria
Sprulac	Sprue, steatorrhea, and coeliac disease
Velactin	Galactosaemia and gluten-free diets for gluten-sensitive enteropathy

The Committee considers that the presence of small quantities of medicaments in toilet preparations does not justify their prescription on form E.C.10. It suggests that disinfectants should be regarded as drugs only when ordered in such quantities and with such directions as are appropriate for the treatment of patients.

The report concludes by acknowledging that there are circumstances in which hardship and suffering would be caused by the rigid application of rules, and advises that the definitions it suggests should not be regarded as inflexible.

* Professor A. G. Macgregor, Chairman; Professor A. H. Beckett, Dr. R. H. Davis, Mr. J. C. Hanbury, Dr. L. Lamont, Dr. M. Hamilton, and Professor D. R. Wood.

REFERENCES

[1] *National Health Service Act*, 1964, S. 38.

[2] Standing Joint Committee on the Classification of Proprietary Preparations. *Report on the Definition of Drugs (Borderline Substances)*, 1967. H.M.S.O. Price 1s. 9d.

ANY QUESTIONS?

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

Medical Contraindications to Oral Contraceptives

Q.—*What precisely are the medical contraindications to oral contraceptive agents in women?*

A.—According to the World Health Organization Report[1] a few rare conditions are known to be aggravated by oral contraceptive administration; these are acquired or hereditary defects of hepatic excretory function, including the Dubin–Johnson and Rotor syndromes. Women who have had idiopathic recurrent jaundice of pregnancy redevelop jaundice if given oral contraceptives. Certain other conditions, for which there is no substantial evidence of adverse reaction to oral contraceptives, but where caution is thought to be advisable, include a history or suspicion of carcinoma of the genital organs and breasts, as well as past or present liver disease without evidence of impaired excretory function. If cardiovascular-renal disease is present, the possible adverse consequences of sodium and fluid retention must be considered.

A number of other conditions have, from time to time, been suggested as contraindications to oral contraceptives, but for these no convincing evidence of cause-and-effect relationship has been adduced. These include thrombo-embolic disease, varicose veins, cerebrovascular accidents, various ophthalmological manifestations (e.g., papilloedema, retinal artery thrombosis, retrobulbar neuritis, visual diminution, and peripheral field restriction) and psychic depressive states. There appears to be no justification for regarding these conditions as contraindications. Nevertheless, there remains the possibility, as with any therapeutic agent, of rare individual idiosyncrasy.

A number of conditions, especially some with a supposedly allergic basis (e.g., asthma, eczema, vasomotor rhinitis, and migraine), and others (such as alopecia, epilepsy, multiple sclerosis, and rheumatoid arthritis), appear to be made worse in some women by the use of oral contraceptives. In other women, however, they appear to be improved.

During lactation the administration of high dosage oral contraceptives should be avoided where continued breast-feeding is desired.

The possible adverse effects of the use of oral contraceptives by women suffering from a variety of common diseases, such as diabetes, tuberculosis, cardiovascular-renal disorders, various parasitic and neoplastic disorders, and malnutrition, require a good deal more investigation before any useful statement can be made.

REFERENCE

1 *Wld Hlth Org. techn. Rep. Ser.*, 1966, 326.

Chromium Contamination of Food

Q.—*Can food cooked in stainless steel saucepans stimulate production of cholesterol through minute traces of chromium getting into food?*

A.—The chromium contamination of food cooked in stainless steel pans was studied in detail by Titus *et al.*,[1] who found that the amount of chromium extracted by the food was extremely small and no toxic effects from this source have been reported. Fairhall[2] points out that the chromium extracted enters solution as chromic salts, and that large amounts of these salts can be given without toxic effect. I have been unable to find any evidence suggesting that cholesterol production would be affected.

REFERENCES

1 Titus, A. C., Elkins, H. B., Finn, H. G., Fairhall, L. T., and Drinker, C. K., *J. industr. Hyg.*, 1930, **12**, 306.
2 Fairhall, L. T., *Industrial Toxicology*, 2nd ed., 1957. Baltimore.

Combining Hypotensive Drugs

Q.—*Are there any contraindications to combining hypotensive drugs in a patient with hypertension who does not appear to respond satisfactorily to one alone?*

A.—Not only is there no contraindication to combining standard hypotensive drugs but in many cases there is a positive advantage in doing so. All these drugs have side-effects, and most side-effects are proportional to dose. By using combinations of drugs each may be employed at a dose short of that which produces side-effects. The only combination which is perhaps unwise is that of methyldopa and reserpine. Both these drugs have depressant effects on the central nervous system, and it is possible that serious depression might arise when using the combination. However, even this has not been established; and there may be agitated hypertensive patients in whom this combination may be more suitable than any other. It is probably somewhat risky to combine the monoamine oxidase inhibitor pargyline with methyldopa; but the known risks of all mono-amine oxidase inhibitors are so great that there is no warrant for their use in hypertension when so many better and safer drugs can be used; so this question should not arise.

Ascorbic Acid Deficiency and Cataract

Q.—*Is deficiency of ascorbic acid a cause of cataract.*[1]

A.—Though ascorbic acid is found in high concentration in the normal lens, cataract has never been reported as a complication of scurvy. There is often a reduced concentration of ascorbic acid in a cataractous lens, but this is morely likely to be an index of lowered metabolism than a cause of cataract.

REFERENCE

1 *The Extra Pharmacopoeia, Martindale*, 1958, 24th ed., **1**, 193. London.

Thiazides in Hypertension

Q.—*What is the mode of action of thiazide and other diuretics in reducing hypertension?*

A.—The immediate hypotensive effect of thiazides depends in part upon an acute reduction of plasma volume, which results in decreased cardiac output and is associated with a slightly increased peripheral resistance. This effect can be prevented by coincident administration of salt, or by expansion of the plasma volume by dextran. This mechanism also provides a satisfactory explanation why thiazides enhance the action of sympathetic-blocking agents,[1] because sympathetic activity is increased consequent upon lowering of the plasma volume.

Nevertheless, haemodynamic studies show that in the course of a few weeks both the plasma volume and the cardiac output return towards normal, despite the continued administration of the drug, but that the blood pressure remains low because of decreased peripheral arteriolar resistance.[2] At this stage replacement of sodium loss does not prevent the hypotensive effect.

The mystery about the mode of action of thiazides has not been settled. It might be an opposite effect to the slowly developing hypertension due to sodium-retaining drugs—which at first raise plasma volume and cardiac output, but within a few weeks increase peripheral resistance, while cardiac output returns to normal.[3] There is much interest at present in the concept that the peripheral circulation has the ability to maintain the blood flow through an organ constant despite variation in perfusion pressure. Recent studies with the thiazide derivative diazoxide, however, suggest that there may be a direct action of thiazides on precapillary resistance vessels,[4] which is completely independent of its effects on renal electrolyte excretion. There is at present not enough information about the thiazide diuretics to be able to decide which of these two possibilities is correct.

REFERENCES

1 Dustan, H. P., Cumming, G. R., Corcoran, A. C., and Page, I. H., *Circulation*, 1959, **19**, 360.
2 Wilson, I. M., and Freis, E. D., ibid., 1959, **20**, 1028.
3 Borst, J. G. G., and Borst-de-Geus, A., *Lancet*, 1963, **1**, 677.
4 Rubin, A. A., Zitowitz, L., and Hausler, L., *J. Pharmacol. exp. Ther.*, 1963, **140**, 46.

Prognosis of Breast Cancer

Q.—*Some people say that it is the site of breast cancer that determines its prognosis, and not its early detection. Is routine screening to detect early cancer of the breast worth while?*

A.—The site of the lesion appears to play some part in the prognosis of breast cancer. It has been reported that patients with growths in the medial half of the breast have a 52% five-year survival rate, compared with 65% for those with growths in the lateral half.[1] This probably results from the involvement of the regional nodes. Only 26% of patients with growths in the centre or inner half of the breast have no involvement of the axillary or internal mammary chain, compared with 33% of those with tumours in the outer half.[2]

Routine screening would probably be worth while (although there is no definite proof of this) if suitable methods existed for carrying it out. Of most promise is a combination of clinical examination and mammography, and a trial of this is being undertaken at the moment in New York.[3] The disadvantages are the frequency of examinations, the time involved, and the cost if such a service was to be provided on a national scale. Much work is now going on to isolate from the normal population those women who stand a greater than normal chance of developing breast cancer. This "high risk group" could then be subjected to frequent clinical and radiological examination.[4]

In the meanwhile it may be prudent to encourage women to examine themselves at intervals, and for the physician always to include an examination of the breasts when a patient is clinically examined for other reasons. Many hospitals now use mammography as a routine screening procedure for those patients who are known to stand a high risk (for example, the opposite breast in women who have already had a mastectomy for cancer) and also those in whom clinical examination is difficult.

REFERENCES

1 Hawkins, J. W., *J. nat. Cancer Inst.*, 1944, **4**, 445.
2 Handley, R. S., and Thackray, A. C., *Brit. med. J.*, 1954, **1**, 61.
3 Shapiro, S., Strax, P., and Venet, L., *J. Amer. med. Ass.*, 1966, **195**, 731.
4 Hayward, J. L., *Proc. roy. Soc. Med.*, 1966, **59**, 1204.

Notes and Comments

Mumps in Pregnancy.—Dr. G. X. TRIMBLE (Medical Director, Catholic Hospitals Medical Education Foundation, Kansas City, Missouri, U.S.A.) writes: In his answer to this question ("Any Questions?" 7 January, p. 38) your expert stated: "There is no evidence that maternal mumps is followed by an increased risk of abnormality in the baby." In support of his statement he cited 1958 and 1960 references. It seems, however, that evidence to the contrary is accumulating. F. J. Plotz,[1] while acknowledging the inconclusive nature of the available data, nevertheless mentioned an incidence of malformations reported by various investigators varying from 6 to 30%. He also cited other studies which suggested that primary endocardial fibroelastosis in children may be the result of a mumps intrauterine infection. Plotz recommends "the administration of pooled gammaglobulin to exposed pregnant women with negative intradermal mumps test results." J. W. St. Geme[2] and his colleagues recently reviewed data which they feel lend support to a relation-

ship between maternal mumps virus infection and endocardial fibroelastosis in the infant. An editorial comment[3] on St. Geme's paper pointed to the inconclusive nature of the evidence and to the need for prospective studies in this specific area. J. Holowach and her associates[4] reported an instance of "congenital chorioretinitis in which the apparent aetiology was foetal mumps virus infection." Moloshok,[5] in a survey of the problem, declared: "The effects of mumps acquired during pregnancy on the foetus is still uncertain because of the relatively small number of prospective studies and the lack of virological investigations on newborns and foetuses."

Granted that the evidence is not definitive, there is enough evidence suggestive of mumps virus teratogenicity, so that the inclusion in your expert's reply of a statement concerning the possibilities would have been appropriate.

OUR EXPERT replies: Clear-cut evidence for an association of mumps and abnormality in the baby can be seen convincingly only from prospective studies. There have, as far as I know, been no such studies since 1960. The retrospective and skin-test evidence of an association between endocardial fibroelastosis and mumps infection in pregnancy (in particular the recent findings of St. Geme *et al.*[2 3] which Dr. Trimble quotes) is intriguing and should have been mentioned, though the association is perhaps not yet certain enough to justify measures of prophylaxis.

REFERENCES
1 Plotz, E. J., *N.Y. St. J. Med.*, 1965, **65**, 1239.
2 St. Geme, J. W., Noren, G. R., and Adams, P., *New Engl. J. Med.*, 1966, **275**, 339.
3 Ibid., 1966, **275**, 393.
4 Holowach, J., Thurston, D. L., and Becker, B., *J. Pediat.*, 1957, **50**, 689.
5 Moloshok, R. E., *Clin. Obstet. Gynec.*, 1966, **9**, 608.

Acquired Koilonychia.—Dr. N. MARSDEN (Senior Casualty Officer, Victoria Hospital, Burnley, Lancs) writes: With reference to the answer to this question ("Any Questions ?" 4 February, p. 287) I wish to add another to your list of causes of acquired koilonychia. I have encountered foundry workers who were obviously not anaemic but who had spoon-shaped deformities of their finger-nails indistinguishable from iron-deficiency koilonychia except for the fact that the patients were in good general health. The cause of the deformity is repeated avulsion of the finger-nails in the course of the foundry worker's occupation. Where only one finger-nail has been avulsed repeatedly the distinction from iron deficiency is usually obvious; but where all the finger-nails have been avulsed the resulting koilonychia could well be confusing, especially if the patient were to present with some debilitating illness.

OUR EXPERT replies: I think this is a very interesting observation. I have not had the fortune to see such a case, and am interested to hear that it can occur.

NEW APPLIANCES

A "Fail Safe" Oxygen Device

Dr. B. G. B. LUCAS, consultant anaesthetist, University College Hospital, London W.C.1, and Mr. L. FISHER, chief engineer and local director, Vickers Research Ltd., Sunninghill, write: A failure in the oxygen supply to an anaesthetic machine may result in the death of the patient. Though a number of warning devices are available, none of them are completely satisfactory, as they do not "fail safe"—that is, they do not take any positive action for the safety of the patient if the oxygen supply fails.

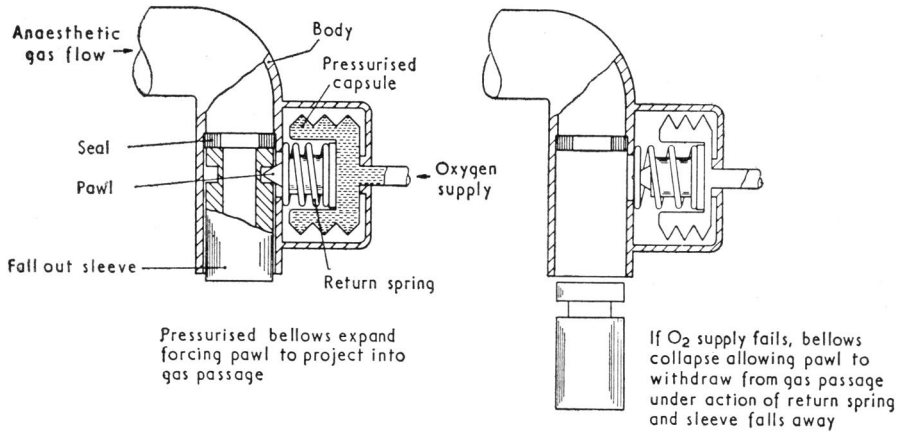

FIG. 1

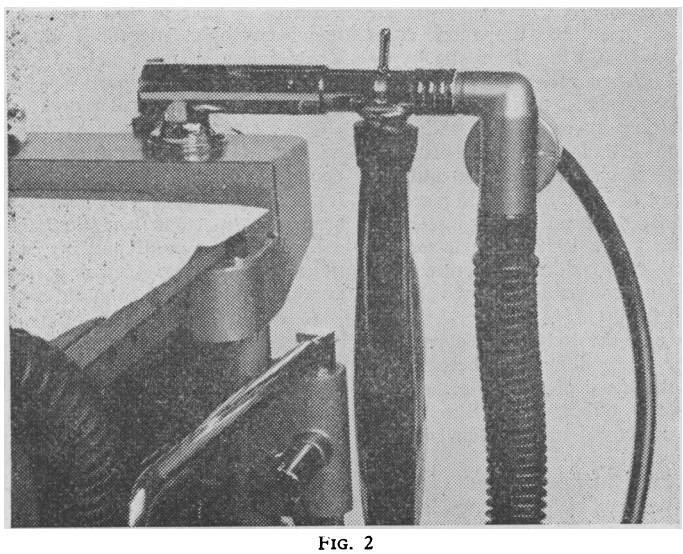

FIG. 2

The apparatus described below was designed primarily as a "fail safe" device and secondly as a warning. The basic principle is that the anaesthetic machine end of the rebreathing tube is held in position by the pressure in the oxygen supply line. Should this fail, the rebreathing tube becomes detached and falls to the floor; the patient can then breathe air, albeit with a greatly increased dead space. The disconnexion provides a visual and probably audible warning, and the rebreathing tube cannot be reattached unless pressure is restored to the oxygen supply line. The device is formed in a shape that makes deliberate retention of the parts by adhesive strapping or other means very difficult. It is robust, requires no maintenance, and is designed to operate when the oxygen line pressure falls below 2.5 lb./sq. in. (0.175 kg./sq. cm.).

The construction is based upon two hot brass pressings which contain the actuating mechanism. This consists simply of a pressure-sensitive bellows, two springs, and a stainless-steel pawl. A pressure tapping is taken from the low-pressure oxygen supply. The pressure expands the beryllium-copper bellows, causing the pawl to project into the outlet gas passage (Fig. 1). A stainless-steel drop-out sleeve is inserted into the outlet until the pawl engages in the groove in the sleeve body. The inward, or engaging, movement of the pawl is spring-loaded, so that the sleeve can be inserted easily regardless of the pressure applied to the bellows. A rubber section provides a gastight seal between the sleeve and the outlet wall.

The device must be fitted in the anaesthetic machine in such a way that its own outlet is vertical (Fig. 2). In the event of a failure of the oxygen supply the pawl is withdrawn by the collapse of the bellows and the action of the return spring, and the sleeve drops away, thereby opening the gas circuit to atmosphere.

This device was made by Oxygenaire Ltd., Basingstoke, Hampshire, from whom further information may be obtained.