indicated: (1) *n*-Propyl gallate (100 parts per million); *n*-octyl gallate (100 p.p.m.); *n*-dodecyl gallate (100 p.p.m.); or any mixture of these three not exceeding 100 p.p.m. (2) Butylated hydroxyanisole (B.H.A.), 200 p.p.m.; butylated hydroxytoluene (B.H.T.), 200 p.p.m.; or a mixture of these not exceeding 200 p.p.m. Mixtures of all these are permitted within limits given in the Food Regulations, 1958.[1]

These antioxidants have not been known to give rise to any toxic effects in fats at the levels indicated. Cases have been reported of skin sensitivity developing among workers handling large quantities of margarine containing gallates.[2 3]

REFERENCES

[1] *Statutory Instrument*, 1958, No. 1454. H.M.S.O., London.
[2] Brun, R., *Berufsdermatosen*, 1964, **12**, 281.
[3] Burckhardt, Von W., and Fierz, U., *Dermatologica (Basel)*, 1964, **129**, 431.

## Unrelated Congenital Defects

**Q.**—*A patient has had three children. The first died at the age of 3½ of an ovarian tumour; the second, a boy, has a coarctation of the aorta; the third, also a boy, had a deformity of the left hand at birth (all the digits of that hand were joined and ended at the first interphalangeal joint). There is no known family history of congenital abnormalities. What are the chances of further children having abnormalities?*

**A.**—The three congenital abnormalities in this family are almost certainly unrelated. The only one with an appreciable recurrence risk is coarctation of the aorta, and here the risk of recurrence is of the order of only 1 to 2%.[1 2]

REFERENCES

[1] Lamy, M., Grouchy, J. De, and Schweisguth, O., *Amer. J. hum. Genet.*, 1957, **9**, 17.
[2] Campbell, M., and Polani, P. E., *Lancet*, 1961, **1**, 463.

# Notes and Comments

**Side-effects of Antidiabetic Drugs.**—Dr. L. J. P. DUNCAN and Dr. B. F. CLARKE (Diabetic and Dietetic Department, Royal Infirmary, Edinburgh 3) write: In connexion with the answer to this question ("Any Questions?" 8 May, p. 1236), we cannot agree with the statement that the type of diabetic being treated with a sulphonylurea compound is unlikely to be a suitable patient for either phenformin or metformin. The type of diabetic referred to, being the insulin-independent, maturity-onset diabetic uncontrolled on diet alone, may be treated by either a sulphonylurea or a diguanide, the choice of drug varying in different countries, and in certain instances both types of drugs may be used in combination. Moreover, the reference quoted[1] contains certain misconceptions both with regard to the pharmacological mode of action of these drugs and to aspects of their clinical use. For instance, it is no longer believed that, *in vivo*, the diguanides inhibit aerobic glycolysis.[2] Likewise the statement that the use of oral hypoglycaemic drugs should be considered in only 10% of diabetic patients does not accord with our own experience or the figures of 30–45% reported from the U.S.A.[3] and West Berlin.[4]

Dr. J. L. JAMES (Department of Medicine, The General Infirmary, Leeds 1) writes: In the answer to this question ("Any Questions?" 8 May, p. 1236) it is stated that a patient under treatment with a sulphonylurea is unlikely to be suitable for treatment with phenformin and metformin and that the indications for the two groups of drugs are different. Reference is made to *To-day's Drugs*[1] in support of this statement, yet there (p. 237) it is stated that diguanides "may be used either alone or in conjunction with a sulphonylurea." Your expert's answer to the question seems to be at variance with this. Perhaps he would say in what way the indications for the two groups of drugs differ in maturity-onset diabetics. The fact that diguanides are not dependent upon functioning islet tissue for their action does not render them ineligible in maturity-onset diabetics, some of whom become refractory to the action of a sulphonylurea used alone.

Dr. J. M. STOWERS (Diabetic Clinic, Aberdeen Royal Infirmary) writes: I was surprised to read your expert's reply to this question ("Any Questions?" 8 May, p. 1236). In his final sentence he expresses doubt that a patient who was responding to the hypoglycaemic action of a sulphonylurea will also respond to the hypoglycaemic action of a diguanide compound such as phenformin or metformin. In fact, I would have said that it was just the sort of diabetic who responds well to the hypoglycaemic reaction of the sulphonylureas who may be expected to respond well to the diguanides, whatever their relative merits in other respects. To suggest otherwise is to disagree with the major publications on this subject and is likely to cause confusion and misunderstanding in the minds of your readers.

OUR EXPERT replies: The criticisms of the commentators seem to be directed more against the statements made in the *To-day's Drugs* article,[1] which I quoted as a reference, than against my reply, which was concerned mainly with the question of drug sensitivity. I would not quarrel with their view that more modern opinion is that for many patients with maturity-onset diabetes either a diguanide or a sulphonylurea compound can be used. What would have been really helpful would have been if any of the commentators could have said whether or not in their experience a patient who had exhibited a sensitivity reaction to one group of antidiabetic drugs could successfully be switched to a drug of the other group.

REFERENCES

[1] *To-day's Drugs*, 1964, p. 237. British Medical Association, London.
[2] Duncan, L. J. P., and Clarke, B. F., *Ann. Rev. Pharmacol.*, 1965, **5**, 151.
[3] Beaser, S. B., *Diabetes*, 1964, **13**, 472.
[4] Bernhard, H., ibid., 1965, **14**, 59.

**Paroxysmal Sneezing.**—Dr. H. MAXWELL (London N.W.7) writes: I was interested in the answer to the question about paroxysmal sneezing ("Any Questions?" 5 June, p. 1483). I have a male patient who can "sneeze to order" as a result of sexual fantasies. The sneeze itself is probably in the nature of an orgasm, and a neurologist has suggested that there could be a connexion between this mechanism and some cases of vasomotor rhinitis. I would be glad to hear your expert's comments.

OUR EXPERT replies: There is some connexion between the nasal mucous membrane and sex, which no doubt accounts for the old wives' description of the honeymoon cold that affects quite a number of newly married couples and causes some nasal obstruction, though I have not heard whether sneezing is included in this.

**Malaria in N. Africa.**—Mr. P. G. SHUTE (Experimental Officer, Malaria Reference Laboratory, Public Health Laboratory Service, Horton Hospital, Epsom, Surrey) writes: It is really surprising that the answer to this question ("Any Questions?" 29 May, p. 1425) failed to advise that prophylaxis should be continued for at least one month from the last day of a possible infection. Indeed, it is beyond all doubt that it is more important to take a prophylactic drug for a month after the last possible chance of being infected than it is during the period of exposure. I have been studying "imported cases" for some years past and now have over 200 records. With a single exception, all the cases of *P. falciparum* occurred among people who stopped taking their prophylactic drug on the day they left Africa or within a few days after arrival home. Also I have investigated all reported deaths, about six over the past four to five years, and in every case the patients discontinued taking their proguanil or chloroquine on the day of departure, and all were from Africa.

Dr. P. H. SHORTHOUSE (Department of Geriatric Medicine, Chesterton Hospital, Cambridge) writes: With reference to this question ("Any Questions?" 29 May, p. 1425), should not anyone taking malaria suppressive medicines be advised to continue them for at least three to four weeks after leaving the area of infection? This is considered as important as starting the medicines two weeks before leaving a non-malarial area.

OUR EXPERT replies: The vast majority of malarial infections originating in Tunisia are due to *Plasmodium vivax*, the 5% or so attributable to *P. falciparum* occurring in oases in the southern part of the country. If a visitor became infected with *P. vivax*, paludrine 100 mg. daily or chloroqine base 300 mg. weekly would normally be adequate for suppression. Prevention of relapse may be achieved either by (1) continued suppression—for example, for a year or longer until the infection dies out spontaneously—or (2) eradication of the infection by giving an 8-aminoquinoline such as primaquine—a treatment which cannot be left in the hands of the patient himself.

Malignant tertian malaria due to *P. falciparum* occurring in the traveller after his return to this country may result during the first few weeks from a liver form of the parasite, but thereafter is more probably due to persistence of blood forms that usually die out spontaneously after a few months. These have, however, occasionally been found a year or more after leaving the endemic area. Suppression continued for a month after returning to this country would certainly prevent relapse in quite a high proportion of cases. The traveller on a short visit to Tunisia would almost certainly be exposed only to *P. vivax*. It should be stressed that this is an infection with little or no mortality.

**Flashlight in Babies' Eyes.**—Mr. F. R. NEUBERT (Guernsey) writes: The answer to this question ("Any Questions?" 5 June, p. 1483) arouses the interest of photographers who do medical photography of the face. A 200-joule tube with a flash duration of 1/10,000 held 5 in. (12.7 cm.) from the face causes practically no after-image, but a flash duration of 1/600th produces an after-image which remained in my own eye for over an hour, obscuring three-quarters of the field of vision, and my colleague, who was working with me, was unable to drive home for nearly half an hour owing to the size and intensity of his own after-image.

I have photographed the conjunctival vessels in many patients with the faster flash without trouble, but it would be interesting to find whether any investigation has been made into the effects of the slow burning flash-bulbs when held a few inches from the eye.

**Correction.**—In the paper on "Surgery of Carotid Artery Stenosis" (5 June, p. 1460), lines 12 and 13 in the second column of p. 1461 should have read ". . . (2) General anaesthesia with plastic-tube bypass from the common to the internal carotid artery . . ." *not* "external carotid artery."