Two dietary factors have been implicated in the parallel aging of tendons and arteries. Schwartz² suggests that the trace element silicon is the factor in dietary fibre and hard water which reduces the incidence of CHD. Silicon contributes to the stability of connective tissue by forming -O-Si-O- bridges. Ascorbic acid is the second factor. Its role in collagen synthesis³ makes it essential for both tendons and arteries.

Our observations on cardiac patients who take up marathon running show a conspicuous increase in silicon-rich foodstuffs (pectin, bran, and alfalfa) and also ascorbic acid (fresh fruit and vitamin C supplements). The longest run for cardiac patients is the Primo 100-km run on the island of Oahu. It is supported by the cardiac rehabilitation programme of the Honolulu YMCA. The event is social and non-competitive.

In our view any dietary manipulation should be aimed at increasing "distance covered on foot."

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¹ Adams, C W M, *et al*, *Atherosclerosis*, 1974, **19**, 429.
² Schwartz, K, *Lancet*, 1977, **1**, 454.
³ Turley, S D, *et al*, *Atherosclerosis*, 1976, **24**, 1.

Paget's disease of bone

SIR,—Your leading article (4 June, p 1427) dismisses glucagon and mithramycin in the treatment of Paget's disease of bone because of disadvantages which were not enumerated.

The dose of mithramycin used by Ryan *et al* was 25 µg/kg/day and was reduced below this only for elderly patients and those with side effects. If the dose of mithramycin used is 15 µg/kg/day patients respond clinically and biochemically and no anorexia, nausea, vomiting, drowsiness, fever, thrombocytopenia, or hepatic damage is encountered.² A dose of 10 µg/kg is also effective. I know of no reports of the use of oral cytotoxic drugs in patients with Paget's disease of bone, but a number of years ago I had the opportunity of observing the effect of azathioprine 50 mg/day for three weeks given to a patient who happened to have Paget's disease of bone. There was no relief of bone pain but both serum alkaline phosphatase and urinary hydroxyproline levels fell gradually. Paget's disease of bone is a relatively common disorder and clinicians should from time to time have opportunities to observe the response of the bone disorder to oral cytotoxics given for other reasons.

Glucagon when given intravenously or subcutaneously is remarkably free of side effects. The only problem encountered in the frequent use of the drug over seven years^{3,4} has been nausea and vomiting, which occurs when large doses of the hormone are given by intravenous infusion. These symptoms are dose-dependent and are rapidly relieved by stopping the infusion for a few minutes, glucagon being rapidly cleared from the blood.⁵ Glucagon when given intravenously at a dose of 8-10 mg/day results in relief of bone pain and a fall in serum alkaline phosphatase and urinary hydroxyproline levels within 10 days. A similar clinical and biochemical response takes many months with calcitonin.

The patient with Paget's disease of bone can be maintained on subcutaneous glucagon

2-3 mg once or twice daily without side effects. Alternatively glucagon can be given in combination with calcitonin and I hope to publish further data on this variation of therapy in due course. Glucagon may actually have some advantages over the calcitonins. Hypocalcaemia is uncommon during glucagon therapy and the hormone may be less likely to give rise to antibodies. Furthermore, I have not encountered a patient with Paget's disease of bone who was resistant to glucagon therapy.

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¹ Ryan, W G, Schwartz, T B, and Northrop, G, *Seminars in Drug Treatment*, 1972, **2**, 57.

² Condon, J R, *et al*, *British Medical Journal*, 1971, **1**, 421.

³ Condon, J R, *British Medical Journal*, 1971, **4**, 719.

⁴ Condon, J R, Knight, M, and Day, J L, *British Journal of Surgery*, 1973, **60**, 509.

⁵ Assan, R, Tchobrousky, G, and Gross, G, Abstract submitted to the meeting of the European Association for the Study of Diabetes, Southampton, September 1971.

Psychotropic drugs and road accidents

SIR,—Your leading article (11 June, p 1492) "Deaths due to drug treatment" made no mention of one possible lethal consequence of drug treatment: road traffic injury. The relationship between the taking of drugs and subsequent accidental injury or death is a field which has attracted little interest or research effort to establish the facts. This is surprising in view of the importance of the matter.

In 1970 in the USA Kibrick and Smart¹ reported that 11-15% of accident-involved drivers had taken a psychotropic drug before the accident. A report of the Medical Commission on Accident Prevention² has reviewed the present situation and summarised the scanty amount of information which has accumulated since Kibrick and Smart published their findings. This report states that "doctors must constantly bear in mind the possibility of adverse drug effects on driving and much will therefore depend upon the information which is available to doctors on this important subject. Unfortunately . . . information about the effects of drugs on driving behaviour is extremely hard to obtain."

The situation as regards the effects of psychotropic drugs and other medications on driving behaviour is certainly complex and little is known with certainty. Clayton³ states that "the role of psychotropic drugs in the causation of driving accidents remains unclear and will remain so until carefully controlled large-scale field studies are undertaken." There is little hard evidence that the acute consumption of a drug with a sedative effect may adversely affect skill in driving and there is practically no knowledge of the effects of chronic consumption of such drugs on driving or other activities requiring a high degree of motor co-ordination and judgment. Yet the evidence incriminating alcohol consumption in impairment of ability to drive is now overwhelming and the response of society to this evidence has been the introduction of the breathalyser.

Sedative drugs, of course, are not detected in the breathalyser and if they were there would be no legal implications. Yet there is good evidence that the sedative drugs commonly prescribed (previously the barbiturates and now the benzodiazepines) do potentiate the

effect of alcohol. A standard work on the side effects of drugs⁴ states that "diazepam has a tendency to produce drowsiness and ataxia. . . . There is a summation effect with alcohol: patients should be warned to be very moderate with alcohol and to take none before driving."

Prescriptions for sedative drugs and hypnotics now run into millions a year. The people to whom they are prescribed are also likely to be using alcohol, perhaps in unaccustomed amounts; yet there is no requirement placed upon the medical profession to issue a warning of this interaction effect when the drugs are prescribed.

We believe that research in this field has been too long delayed and that it should now be accorded priority. Until such time as definite information is available to guide doctors we consider that it should be made obligatory to issue warnings of interaction effects with alcohol whenever sedative drugs are dispensed. Complaints may be made that issuing such warnings and recommendations will inevitably decrease treatment compliance, but if this is to be set against the potential saving of life then the balance will be favourable, for sedative drugs are frequently prescribed for relatively trivial reasons. If the concealed dangers were to be forcibly pointed out to patients and to doctors, then it would increase the chances that they are only prescribed for, and taken by, those patients who really need them.

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¹ Kibrick, E, and Smart, R G, *Journal of Safety Research*, 1970, **2**, 73.

² *Drugs and Medicines* (reprinted from *Medical Aspects of Fitness to Drive*, 3rd edn). London, Medical Commission on Accident Prevention, 1976.

³ Clayton, A B, *Human Factors*, 1976, **18**, 241.

⁴ Meyler, L, and Herxheimer, A, *Side Effects of Drugs*, vol 7. Amsterdam, Excerpta Medica, 1972.

Abdominal tuberculosis in Britain

SIR,—Your leading article (18 June, p 1557) reminds us that abdominal tuberculosis still occurs in the indigenous population of the United Kingdom. Gynaecologists would do well to recall its possibility, particularly in Asians but also in other races. Four cases have been seen in a short personal experience in the West Midlands. The fourth and most recent one illustrates how difficult it can be to establish the diagnosis, however great the clinical suspicion.

An Asian woman, 22 years of age, was seen at the 30th week of her first pregnancy because the uterus was larger than expected. An x-ray of the abdomen confirmed the presence of twins. The patient was admitted to hospital because she looked ill and weighed only 44 kg. The haemoglobin concentration was 12.3 g/dl and the chest x-ray normal. Labour started spontaneously at the 35th week and she was delivered of living twins (1.68 kg and 1.75 kg). Within 48h pyrexia with marked tachycardia developed and anaemia, jaundice, and hepatomegaly followed. The haemoglobin fell to 8.1 g/dl with 8.6% reticulocytes and the urine was free of bile. The plasma albumin concentration fell to 25 g/l and that of globulin rose to 38 g/l, while the alkaline phosphatase activity rose to 95 King Armstrong units. A pure growth of *Escherichia coli* was obtained from the urine and a high vaginal swab. Initial blood cultures were sterile. Antibiotic therapy was commenced. By the 10th day the

patient was confused, which was attributed to a severe electrolyte imbalance. Repeat x-rays of the chest and abdomen revealed no abnormality, although by now an ill-defined swelling was palpable in the right lumbar area.

At this time the diagnosis was thought to lie between abdominal tuberculosis, repeated internal haemorrhages, appendix abscess, and peritonitis due to bacteroides infection. Laparotomy revealed pus in the right paracolic gutter with adhesions: the right tube was grossly inflamed, while the left tube and appendix were both normal. The pus grew *Staphylococcus aureus* and *Bacteroides* spp. Treatment with clindamycin and metronidazole was started. The patient remained very ill and her weight fell to 32.2 kg. Blood (2.2 l) was transfused to correct the anaemia. By the 19th day the patient was deteriorating, with a swinging pyrexia. A Heaf test was doubtfully positive. Blood culture now grew *Staph aureus*. No malaria parasites could be found. The Widal reaction was negative. Yet another chest x-ray showed clear lung fields and repeated scanning showed no evidence of a sub-phrenic abscess. The fluorescent amoebic antibody test was negative. The patient became critically ill. Apart from cachexia and moderate tenderness in the right hypochondrium pyrexia and tachycardia were the dominant signs. There was no leucocytosis. The Heaf test was now definitely positive, but the fundi were considered normal. Anti-tuberculosis therapy was started with ethambutol, isoniazid, and rifampicin. Just at this time a chest x-ray showed miliary tuberculosis, 46 days after delivery. Recovery was dramatic, the pyrexia and tachycardia settling within eight days. Fourteen weeks later the patient was discharged from the tuberculosis unit fit and well.

In all, just over 100 pathology and radiology reports were filed before the diagnosis was made, when peritoneal biopsy¹ or even possibly salpingectomy would almost certainly have revealed the true state of affairs.

I thank Dr Roger Williams for making the diagnosis and Dr J T Hutchison for curing the patient's tuberculosis. Guy's Hospital Medical School kindly performed the fluorescent amoebic antibody test.

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¹ Das, P, and Shukla, H S, *British Journal of Surgery*, 1976, **63**, 941.

Campylobacter enteritis

SIR,—Dr M B Skirrow (2 July, p 9) is to be congratulated on drawing attention to campylobacters as a cause of enteritis.

Our investigations have led us to believe that the reservoir of the organisms is the wild bird population and that they are transmitted to humans by healthy poultry, meat, and possibly even by other foodstuffs contaminated with bird droppings and inadequately cleaned.

In the United States Smibert¹ isolated campylobacters (*Vibrio fetus* var *intestinalis*), from the intestinal contents of 11 of 15 sparrows, one of nine starlings, one of five pigeons, and one blackbird which he had trapped in and around sheep and cattle barns. He also isolated the organisms from the intestinal contents of sheep, aborted ovine fetuses, the intestinal contents of turkeys with transmissible enteritis, and the bile of chickens with vibronic hepatitis.

We have been informed that vibronic hepatitis in chickens is virtually non-existent in the United Kingdom and our preliminary investigations suggest that the organisms are commonly found in the intestine of healthy birds. Recently we examined the caecal contents of 50 freshly killed and apparently

previously quite healthy chickens and found campylobacters in seven (14%). Vacuum packing could provide one of the conditions necessary for their multiplication.

When a discovery like Dr Skirrow's is made there is always the danger of over-reaction, and it is important for us to keep things in perspective. Chickens are now our biggest source of animal protein. Salmonellas may be isolated from more than 30% of those subsequently offered for sale. We are not complacent and there is more work to be done, but, as Dr Skirrow indicates, it is logical to expect the food hygiene measures which have been advocated for the prevention of salmonellosis to control enteritis caused by campylobacters.

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¹ Smibert, R M, *American Journal of Veterinary Research*, 1969, **30**, 1437.

"Measles" in previously immunised children

SIR,—Doctors are often bothered by measles-like rashes in children with a history of live measles vaccination. Professor J A Dudgeon has recently (2 July, p 44) stressed the need "to carry out some virological tests to try and determine whether such cases were in fact measles or resulted from other viral infections."

An investigation by Gerike and Sandow has already given an answer.¹ The authors studied serologically 247 cases of presumed vaccine failures. Only 60 cases (24.3%) could be identified as measles, 100 cases (40.5%) showed at least a fourfold increase in the titre of rubella antibodies, and the remaining 87 cases (35.2%) were undiagnosed. Vaccine failures are therefore more rare than some doctors suppose.

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¹ Gerike, E, and Sandow, D, *Deutsches Gesundheitswesen*, 1976, **31**, 1949.

Bromocriptine and TRH-induced growth hormone release in anorexia nervosa

SIR,—Thyrotrophin-releasing hormone (TRH) has been shown to stimulate the release of growth hormone (GH) in some patients with anorexia nervosa (AN),¹ in contrast to normal subjects. As bromocriptine lowers the raised plasma GH levels in an oral glucose tolerance test (OGTT) in AN² the effect of the drug on TRH-induced GH release was studied for comparison.

Six female patients aged between 15 and 36 years with typical AN³ and weighing between 50 and 88% of their standard weights were studied. After an overnight fast 500 µg of TRH (Roche) was injected intravenously. Blood samples for GH assay were withdrawn through an indwelling needle immediately before and at intervals of 20, 30, 60, 90, 120, and 180 min after the injection of TRH. The patients were then started on treatment with bromocriptine, initially 2.5 mg daily with food and increasing by 2.5 mg every three days to a maximum of

Plasma GH levels (µg/l) following intravenous injection of TRH (500 µg) in six patients with anorexia nervosa before and during treatment with bromocriptine

Patient	Before treatment		During treatment	
	Basal	Peak	Basal	Peak
1	18	36	15	17
2	13	15.3	6.8	14.1
3	56	72	19	27
4	2.7	6.6	1.6	5
5	17	18	14	25
6	2.2	8.8	9.3	6.2
Mean ± SEM	18.2 ± 8	26.1 ± 10	11 ± 2.6	15.7 ± 3.8

Before treatment paired *t* test showed that the difference between the basal and peak levels is probably significant (*P* < 0.05) but no significant difference was found between the basal levels or peak levels before and during treatment or between basal and peak levels during treatment.

10 mg/day. After 14 days' treatment in hospital without changing the dietary regimen the tests were repeated. Plasma GH was measured by specific radioimmunoassay.⁴

The basal and peak plasma GH levels before and during treatment with bromocriptine are shown in the table. Using the same criteria as Maeda *et al*¹—namely, a twofold or greater increase in plasma GH over the basal level and an increment greater than 5 µg/l—two patients (Nos 1 and 6) showed a rise in plasma GH levels before treatment only. One patient (No 2), however, had a rise in plasma GH concentration while on treatment which did not occur before treatment. In addition, we would normally have considered a rise in plasma GH to have occurred in patients 3 and 4 before treatment and patients 3, 4, and 5 after treatment, all these results implying that any rise in plasma GH in response to TRH is not affected by bromocriptine.

It is unlikely that the dose of bromocriptine, 10 mg/day, was so low that this would account for its failure to depress the response to TRH, since the same dose lowered plasma GH levels significantly during an OGTT in patients with AN.²

These results suggest that bromocriptine does not suppress GH release in AN in whole or in part by a direct action on the somatotroph, since stimuli such as TRH are able to bypass any such potential effect of the drug.

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¹ Maeda, K, *et al*, *Acta Endocrinologica*, 1976, **81**, 1.
² Harrower, A D B, *et al*, *British Medical Journal*, 1977, **2**, 156.

³ Lundberg, P O, *et al*, *European Journal of Clinical Investigation*, 1972, **2**, 150.

⁴ Schalch, D S, and Parker, M L, *Nature*, 1964, **203**, 1141.

Survival of specialist societies

SIR,—Scientific medical societies have proliferated with increasing specialisation. In order to keep up to date and maintain contacts many doctors have found it essential to belong to six or more societies and the cost of regularly attending scientific meetings seemed reasonable until recently. Now inflation, high taxation, and frozen earnings are making it financially impossible for most to travel long