

influence of factors other than dietary-fat intake and plasma lipids. The role of endogenous hormones in middle-aged men should perhaps be considered.⁴

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Voice restoration after laryngectomy

SIR—Johnson in his commentary (Feb 19, p 431) should have mentioned not only that many people who acquire a good voice after tracheo-oesophageal puncture and valve insertion would have developed good oesophageal speech anyway, but also that there is a substantial complication rate—eg, osteomyelitis of the cervical vertebrae,¹ retropharyngeal abscess, and carotid haemorrhage.² A patient on our unit, after a rather traumatic puncture, developed mediastinitis and a right pleural effusion, which required long-term intravenous antibiotics, chest drain insertion on three occasions, and three computed tomographic scans. She has spent 71 days of the past 7 months in hospital and still has no voice—the non-functional Provox valve having been removed—and a persistent tracheo-oesophageal fistula. The cost of treatment so far is about £20 000. Maybe this is one of the subjects that head and neck surgeons should consider in a country-wide audit, to see whether the benefits to some justify this high cost to others.

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Deaths from methadone and heroin

SIR—The UK Home Office Statistical Bulletin published in (London: HM Stationery Office, table 20 and p 53) reveals these figures for heroin and methadone deaths:

	1982	'83	'84	'85	'86	'87	'88	'89	'90	'91
Heroin	11	13	24	19	16	22	24	36	34	44
Methadone	16	24	24	9	15	46	37	35	69	74

These figures give a total for the decade of 243 heroin deaths and 349 methadone deaths. In the same bulletin, notified addicts (overwhelmingly to opioids) totalled 24 700. At least 40% of notifications, it continues, are now of addiction to methadone, suggesting 9880 methadone addicts. Given that notifications register, at most, about one-fifth¹ of all addicts, the total addict population in the UK is at least 123 500. If 9880

are addicted to methadone, this leaves 113 620 addicted to heroin; a tiny proportion will be addicted to other notifiable opioids such as dextromoramide (Palfium) or morphine.

In 1991, 44 heroin deaths out of 113 620 addicts yields a mortality of 1 in 2582; 74 methadone deaths of 9880 gives a mortality of 1 in 134. Thus methadone would appear to be 19 times more toxic than heroin, similar to previous findings in New York.² Yet methadone is a manufactured pharmaceutical product whereas heroin is usually adulterated from the "street".

Police surgeons in London³ find that prescribing of methadone syrup by London's doctors is ineffective in stopping illicit drug use and, worse, the methadone is sold on. Furthermore, methadone produces disturbances of weight, sweating, sleep; and dysphoria, in addition to greater numbers of fatalities.^{2,4,5} Given the dangers of methadone and its apparent ineffectiveness, perhaps the current vogue for methadone in the management of addiction should be reviewed.

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Prostate cancer

SIR—Labrie is a great scientist who has made major contributions to prostate cancer treatments, but he is wrong in his report (Feb 19, p 491) about the adrenal glands being "... responsible for close to half the total androgens in adult men and not a 'small extent' ...". My reference works (DeGroot, *Endocrinology* 1989, p 2146; Campbell, *Urology* 1986, p 248; and Lepor et al, *Prostate diseases* 1993, W B Saunders, p 62) all indicate that a very low percentage comes from the adrenal cortex, as does my personal experience. I am a white male, age 75, weight 175 lbs, height 6 feet, diagnosed with stage B prostate cancer, Gleason's grade 2 cells, on Nov 16, 1993. My prostate-specific antigen (PSA) was 10.5 ng/mL and my testosterone 341 ng/dL (normal = 300–1000) on Dec 2, 1993. I had bilateral orchiectomy on Dec 8, 1993, and on Jan 6, 1994 had a testosterone of less than 20 ng/dL and a PSA of 1.9 ng/mL. The orchiectomy had knocked out the prostate cancer and at least 94% of my androgens. The remaining 6% were coming from my adrenal glands.

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Authors' reply

SIR—Cheney's comments are in perfect agreement with textbooks. However, textbooks do not contain the newest knowledge. In fact, information on the formation of androgens and oestrogens in peripheral tissues from the inactive adrenal precursors dehydroepiandrosterone (DHEA) and DHEA sulphate (DHEA-S)¹ is not yet in textbooks.

The residual 5% testosterone serum concentrations after medical (luteinising hormone releasing hormone [LHRH] agonist) or surgical castration result from some leakage of testosterone into the circulation from peripheral tissues where

androgen is made locally from DHEA and DHEA-S. Its concentration in these tissues is much higher than in the serum since these tissues make androgens for their own use. These androgens act in the cells where synthesis takes place—this new area of endocrinology is called intracrinology.¹ The testis, on the other hand, makes and releases androgens for use by other tissues, which are reached by way of the general circulation. Consequently, blood concentrations of testosterone are a valid index of testosterone formation by the testicles but not by peripheral tissues, which leak only a small fraction of active androgens in the blood. Thus, serum concentrations of testosterone are not an appropriate index of androgenic activity; intracellular levels of testosterone and dihydrotestosterone are the only important indices.^{2,3}

Localised prostate cancer is more sensitive to androgen deprivation than more advanced disease. Removal of 60% of androgens as achieved by bilateral orchiectomy is expected to cause an important regression of stage B cancer. More rapid, more complete, and more long-lasting inhibition of prostate cancer is expected with combination therapy when the androgens of both testicular and adrenal origins are blocked simultaneously by surgical or medical castration in association with a pure anti-androgen of the class of flutamide.³⁻⁵ The objective of prostate cancer therapy should not be to obtain a significant response but to reach the best possible response.

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***Bartonella (Rochalimaea) quintana* isolation in patient with chronic adenopathy, lymphopenia, and a cat**

SIR—*Bartonella (Rochalimaea) quintana* causes trench fever. It is transmitted by body lice and has been successively named *Rickettsia quintana*, *Rochalimaea quintana*, and *Bartonella quintana* based on 16S rRNA sequencing.¹ It has been reported as a cause of bacillary angiomatosis, hepatitis peliosis, and endocarditis in AIDS patients.² We report here a case associated with chronic lymphadenopathy.

A 30-year-old woman presented with cervical adenopathy. She noted the adenopathy in 1991 and consulted in 1993 because the glands had increased in size. She was afebrile. Total body computed tomography was done which showed mediastinal lymphadenopathy. She had 4.5×10^9 white blood cells per L and 0.136×10^9 T8 cells per L. Histological examinations of cervical lymph node specimens and of the bone marrow showed a granulomatous reaction. Regular bacteriological cultures of the lymph node and blood remained sterile. Two blood cultures sampled at 2 weeks' interval were inoculated on human embryonic lung cells and human endothelial cell line ECV 304.³ After 10 weeks of inoculation, a weakly gram-negative rod was isolated from both blood

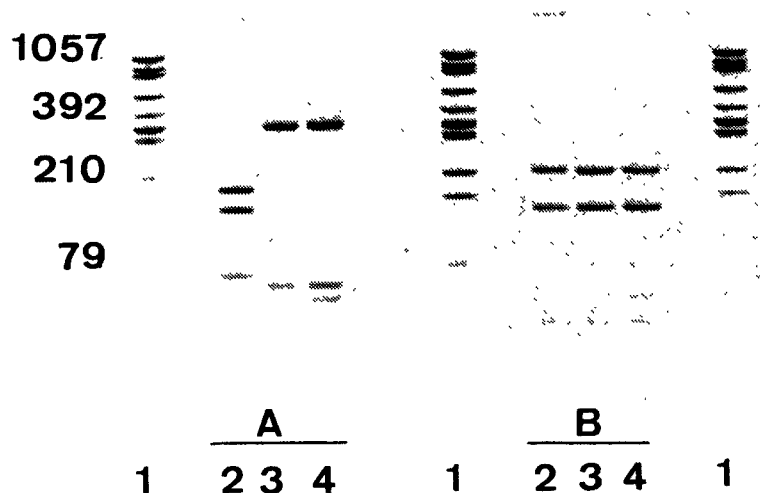


Figure: Restriction profiles of PCR-amplified products of part of citrate-synthase gene

Panel A, *TaqI* digestion; panel B, *MseI* digestion. Lane 1, *Phi X174 HincII* digest as molecular weight marker (molecular weights expressed in base-pairs); lane 2, *Bartonella (Rochalimaea) henselae* digest; lane 3, *Bartonella (Rochalimaea) quintana* digest; lane 4, isolate's digest.

samples and was subcultured onto blood agar. The 16S rRNA sequence of the first isolate had a 100% homology with that of *Bartonella quintana*, but the restriction profiles of the citrate-synthase primer pair amplification previously reported for *Bartonella* identification diverged from that of *Bartonella quintana* when *TaqI* and *MseI* restriction enzymes were used (figure). Specific mouse polyclonal antibody to *Bartonella quintana* reacted with this isolate as well as with the Oklahoma reference strain.⁴ We failed to amplify *Bartonella* from the lymph node. The sera were tested against *Bartonella quintana* Oklahoma strain and the isolate and did not react by immunofluorescence assay. The patient was re-interviewed after characterisation of the isolate and she reported having a cat at home but did not mention a scratch or bite.

We isolated and characterised an atypical *Bartonella quintana* isolate that was different from previous isolates because of its unique citrate-synthase restriction profile. The clinical features of the patient were interesting. She presented with chronic cervical and mediastinal lymphadenopathy and lymphopenia. We cannot confirm if the presence of the cat is relevant or not, but she did not have a typical clinical presentation of cat scratch disease (CSD). This observation, however, has to be correlated with the fact that *Bartonella henselae* can cause bacillary angiomatosis and CSD. Our data imply that *Bartonella quintana* is able not only to cause trench fever and bacillary angiomatosis but also isolated lymphadenopathy.

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