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continuous cell line H-9 (kindly provided by Dr R. C. Gall[3]). Mononuclear cells stimulated with PHA for 3 days were further propagated in medium B (RPMI 1640 with 10% fetal calf serum, 10% T-cell growth factor, and 1/5000 diluted goat antibody to human interferon). Rifabutine (Farmitalia) is poorly soluble in water so methanol was used as solvent.

Virus replication was evaluated by measuring RT activity in the supernatants of the infected cultures. Rifabutine, at 0·1 and 0·5 μg/ml concentrations added daily to the culture medium, inhibited virus production by PHA-stimulated infected lymphocytes by 90–99% (table I).

We also tested the effect of single doses of rifabutine (table II). Uninfected PHA-stimulated lymphocytes and virus-infected lymphocytes at 10^6 cells/ml were incubated with rifabutine 0·1–20 μg/ml in medium B. Parallel cultures were incubated with equivalent volumes of methanol in medium B to evaluate the toxicity of the solvent. After 7 days live cells were counted by the trypan-blue exclusion test and virus production was measured by RT assay. Rifabutine inhibited about 70% of virus production at 10 μg/ml in lymphocytes and at 50 μg/ml in the H-9 cell line. Rifabutine in suspension (without methanol) was inhibitory but to a lesser extent than rifabutine in solution. The concentrations of methanol used had very little effect on live cell counts.

TABLE I—VIRUS-INHIBITORY EFFECT OF LOW DAILY DOSES OF RIFABUTINE

	RT activity		
Rifabutine (μg/ml)	RT (cpm/ml)	% inhibition	Live cells (/ml)
0	$1·54\times10^6$	0	$0·94\times10^6$
0·1	$0·12\times10^6$	92·0	$0·95\times10^6$
0·5	$0·02\times10^6$	99·7	$0·93\times10^6$

PHA-stimulated lymphocytes were infected and treated simultaneously. Drug was added every 24 h. RT activity and cytotoxicity were measured after 7 days.

TABLE II—VIRUS-INHIBITORY EFFECT OF SINGLE DOSES OF RIFABUTINE

Lymphocytes infected* with HTLV-III			Persistently infected H-9 cells		
Rifabutine (μg/ml)	% inhibition of RT activity	Live cells (/ml)	Rifabutine (μg/ml)	% inhibition of RT activity	Live cells (/ml)
0	0	$0·95\times10^6$	0	0	$1·0\times10^6$
0·1	28	$1·0\times10^6$	20	35	$1·2\times10^6$
1	35	$0·90\times10^6$	50	66	$0·96\times10^6$
10	72	$0·95\times10^6$	100	90	$0·85\times10^6$
20	85	$0·88\times10^6$			

*PHA-stimulated lymphocytes were infected and treated simultaneously. RT activity and cytotoxicity were measured seven days after treatment.

Rifabutine has in-vitro activity against *Mycobacterium avium* complex (MAC)[4,5] organisms and it has been suggested that this drug inhibits some mycobacteria by interfering with prokaryotic DNA-dependent RNA polymerase.[4] Some AIDS patients with disseminated MAC infection are now being treated with rifabutine, but the efficiency of this agent against HTLV-III in vivo has not been tested. In volunteers rifabutine penetrates tissues, persists at measurable levels in plasma for 24 h after a single oral dose, and has low toxicity. Peak concentrations of 0·2–0·5 μg/ml in plasma are easily achieved in man 4 h after 75–300 mg doses,[6] and at 24 h or more concentrations are still 0·25 μg/ml. Thus drug levels required for 99% inhibition of viral activity in vitro are achievable by a regimen known to be essentially non-toxic in patients with AIDS-related MAC infection.

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1. Wu AM, Gallo RC. Interaction between murine type-C virus RNA-directed DNA polymerase and rifamycin derivatives. *Biochim Biophys Acta* 1974; **240:** 419–36.
2. Kalyanaraman VS, Chorba T, Getchell JP, et al. Antigenic characterization of human T-lymphotropic virus (HTLV-III/LAV CDC 451) isolated from a patient with AIDS and distribution of HTLV-III/LAV antibodies within human sera. *J Infect Dis* (in press).
3. Popovic M, Sarngadharan MG, Read E, Gallo RC. Detection, isolation and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. *Science* 1984; **224:** 497–500.
4. Woodley CL, Kilburn JO. In vitro susceptibility of *Mycobacterium avium* complex and *mycobacterium tuberculosis* strains to a spiro-piperidyl rifamycin. *Am Rev Resp Dis* 1982; **126:** 586–87.
5. Bruna CDC, Schioppacassi G, Ungheri D, Jabes D, Morvillo E, Sanfilippo A. LM 427, a new spiropiperidyl rifamycin: in vitro and in vivo studies. *J Antibiot (Tokyo)* 1983; **36:** 1502–06
6. Mozzi E, Germiniani R, Cantaluppi G, Marchetti V, Veltaro MP, Sandi A. Human pharmacokinetics of LM 427, a new antimycobacterial agent: tissue distribution and excretion. In: Proceedings of 13th International Congress of Chemotherapy (Vienna, Aug 28–Sept 2, 1983).

ISOLATION OF MONKEYPOX VIRUS FROM WILD SQUIRREL INFECTED IN NATURE

SIR,—Monkeypox virus was first isolated in 1958, from captive monkeys and several outbreaks of monkeypox have been recorded in Europe and the United States in colonies of primates, mainly imported from Asia. In 1970 monkeypox virus was isolated from a child in Zaire,[1] and by Nov 4, 1985, the World Health Organisation's human monkeypox inventory had recorded 310 cases seen in the tropical rain forest of west and central Africa, most of them being in Zaire. Research on the natural host for this virus naturally focused at first on monkeys. In 1969–71 nearly 1200 sera from several species of Asian monkey were tested by haemagglutination inhibition (HI) and neutralisation tests for orthopoxvirus antibodies; all were negative. Nor were antibodies detected in 1447 sera of monkeys imported mainly from the savannah areas of Africa.

Subsequently, the collection of animals narrowed to areas where human monkeypox had been reported. Orthopoxvirus antibodies were found in 8–28% of forest-dwelling primates of west Africa,[2,3] and monkeypox-specific antibodies were identified in three species. A large-scale virus ecology survey in 1979 in Zaire covered a much larger range of wild animals of forty-three species, including monkeys, arboreal and terrestrial rodents, and bats. Orthopoxvirus antibodies were found in between 2% and 70% of various groups of animals, being in some species of monkey, in squirrels, and in one species of terrestrial rodent. Further testing of the positive samples from squirrels revealed monkeypox-specific antibodies in sera of *Funisciurus anerythrus* (J. H. Nakano, personal communication). No monkeypox virus was isolated from organ samples.

From 1984 virus ecology research was further modified by narrowing the focus to the surroundings of villages where human cases had been repeatedly recorded or to the homes of active cases and by collecting all species of animal inhabiting suspected sites. In July, 1985, a joint Government of Zaire/WHO epidemiological team did a survey in northern Zaire, looking for human cases and collecting animals within 40 km of Yambuku, Bumba zone. (Yambuku was affected by an outbreak of Ebola haemorrhage fever in 1976.) 1 of 383 animals sampled, a squirrel *(Funisciurus anerythrus),* found 300 m from a village where a human monkeypox patient had been recorded in 1981, had skin eruptions. Serum, skin, and organs of this animal were tested by two WHO reference laboratories—namely, the poxvirus laboratory, Centers for Disease Control, Atlanta, USA, and the laboratory of smallpox prophylaxis, Research Institute for Viral Preparations, Moscow, USSR. Both laboratories isolated monkeypox virus from the skin and lungs, spleen, and kidneys. The orthopoxvirus antibody titre was 12 726 (by radioimmunoassay) and monkeypox-specific antibodies were identified in serum by radioimmunoassay adsorption (RIAA) test. The virus was also tested by monoclonal antibodies and found identical to monkeypox virus from an infected patient. This is the first time that monkeypox virus has been isolated from an animal infected in the wild.

Another squirrel of the same species captured during the survey near a village where human cases were reported in 1981, 1982, and 1984, had specific antibodies to monkeypox virus. Thus 2 (out of 18

animals of this species sampled) were seropositive and 1 of them was in an active stage of illness. Of 172 terrestrial rodents tested none had monkeypox-specific antibodies. The samples from 51 *F anerythrus* squirrels collected in 1979 have recently been tested by RIAA in Atlanta; 5 had monkeypox-specific antibodies. *F anerythrus* seems to be a priority species in the research on the host reservoir of monkeypox virus.

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1 Ladnyi ID, Ziegler P, Kima A. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. *Bull WHO* 1972; **46:** 593–97.
2. Breman JG, Bernadou J, Nakano JH. Poxvirus in West African nonhuman primates: Serological survey results. *Bull WHO* 1977; **55:** 605–12.
3. Gispen R, Brand-Saathof B, Hekker AC. Monkeypox-specific antibodies in human and simian sera from the Ivory Coast and Nigeria. *Bull WHO* 1976; **53:** 355–60.

COURVOISIER'S LAW

SIR,—Ludwig Courvoisier, and his eponym, have been the subject of much misunderstanding and confusion, both at the bedside and in print. One textbook has labelled him "a pathologist" (a slur on any self-respecting surgeon),[1] and he has also been described as French when, in fact, he was German.[2] Mr Watts (Dec 7, p 273) in his article on Courvoisier's law, writes that "we tend to forget that most classic descriptions were based on meticulous observation of a mere dozen cases". Courvoisier reported on 187 patients with common bileduct obstruction (87 from stone and 100 from other causes such as cancer of the pancreas and strictures). The gallbladder was enlarged in 20% of patients with gallstone obstruction and in 92% of cases with obstruction from other causes.[3] More recent studies on patients with pancreatic carcinoma[4] and a retrospective study looking at the validity of Courvoisier's law[5,6] have confirmed the general trend of Courvoisier's observations, although the discriminative value of the test does not warrant the term "law" (a term not originated by Courvoisier). Chung's study[7] on in-vivo intraoperative ductal pressures and in-vitro distensibility of gallbladders removed at surgery suggests that high-grade obstruction over a prolonged period (more likely with pancreatic carcinoma, but also possible with stones) is responsible for the dilated gallbladder. These studies do not justify Watts' conclusion that "The Law is not true". Clarity might be restored to this murky field by changing the eponym to the "Courvoisier gallbladder", referring to a palpable gallbladder in a jaundiced patient with extrahepatic obstruction. This should be interpreted as probable high-grade obstruction over a prolonged period of time. The actual cause, be it cancer of pancreas or stone, would reflect the population being dealt with and the prevalence of these two diseases. To cite Courvoisier: "if further evidence of this can be found, this would be an important marker for differential diagnosis".[3]

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1. Watson CJ Jaundice: Compelling clinical signs and some differential laboratory aids. In: Najarian JS, Delaney JP, eds. Surgery of the liver pancreas and biliary tract. New York: Stratton International, 1975: 357–69.
2. Veillon E. Professor Dr med L. G. Courvoisier. *Schweiz Med Wschr* 1918; **43:** 1314–19.
3. Courvoisier LG. Kasuistisch-statistische Beitraege zur Pathologie und Chirurgie der Gallenwege Leipzig: Vogel, 1980: 57–59.
4 Mikal S, Campbell AJA. Cancer of the pancreas: Diagnostic and operative criteria based on 100 consecutive autopsies. *Surgery* 1950, **28:** 963–67.
5. Viteri AL. Courvoisier's law and evaluation of the jaundiced patient. *Tex Med* 1980; **76:** 60–61.
6. Ronai PM, Baker RJ, Beller PJ, Anderson PJ, Lander M. Technetium-99m-pyridoxylıden eglutamate: a new hepatobiliary radiopharmaceutical: II Clinical aspects. *J Nucl Med* 1975; **16:** 728–37.
7. Chung RS. Pathogenesis of the "Courvoisier gallbladder". *Dig Dis Sci* 1983; **28:** 33–38

PRIVATE NURSING HOMES AND THE OLD

SIR,—Your Dec 14 editorial raises several important issues arising from the expansion of private sector nursing homes. During 1984, shortly after Department of Health and Social Security supplements for private nursing home residents became widely available, we surveyed 400 patients in eighteen registered nursing homes in Edinburgh.[1] 42 patients (10·5%) were receiving supplementation, and of the 132 admitted after the November, 1983, change in regulations[2] 26·5% were being supplemented. Since March, 1984, there has been a 36% expansion of registered nursing home beds caring for the elderly within Edinburgh, and in one large development recently opened about 50% of patients were receiving DHSS support. It is a matter of great concern that supplementation is based solely on the patient's financial state, and does not require any form of independent medical assessment. Indeed, such an assessment (by a geriatrician or psychogeriatrician) would be in many patients' interests regardless of the appropriateness of DHSS support. A questionnaire sent to Edinburgh general practitioners indicated that 68% (84/124) thought that such an assessment would be beneficial. Assessment by the geriatric services before admission to local authority homes is of value,[3] and is already standard practice in many areas.

There have been few studies of patient dependency in registered nursing homes, but such information as is available[4,5] supports our findings that patients in nursing homes are significantly less dependent than those observed in geriatric continuing care wards. This must in part account for the cheaper costs in the nursing home sector. Furthermore we found that when additional services, such as laundry, chiropody, hairdressing, and physiotherapy, were available the patient usually had to pay for them; this could be a disadvantage to supplemented patients. In Edinburgh, long-term geriatric NHS patients receive these services as part of their care. Nursing homes also experience difficulty in obtaining satisfactory incontinence appliances and certain walking aids. While there may well be a place for developing the nursing home sector to care for the increasing numbers of dependent elderly, the pitfalls of such expansion in terms of patient care and value for money need further consideration.

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1. Primrose WR, Capewell AE. A survey of registered nursing homes within the City of Edinburgh. *J Roy Coll Gen Practit* (in press).
2. Supplementary Benefit (requirements, resources and single payments) amendment regulations. SI: 1399. London: HMSO, 1983.
3. Brocklehurst JC, Carty MH, Leeming JT, Robinson JM. Medical screening of old people accepted for residential care. *Lancet* 1978; ii: 141–43.
4. Wright K. Contractual arrangements for geriatric care in private nursing homes: Discussion paper 4. Centre for Health Economics, University of York, 1985.
5. Wade B, Sawyer L, Bell J. Dependency with dignity. London: Bedford Square Press, 1983.

SIR,—One danger in the expansion of private sector nursing homes is the absence of any independent assessment, so that the DHSS may sometimes be paying for unnecessary institutional care. Reliance on the private sector poses particular problems in the London area, where the high cost of housing pushes up the charges of nursing and residential homes well beyond the allowances that would suffice elsewhere. This pressure, combined with astonishing cuts in the NHS now being demanded of London and with cuts in local government expenditure, means that disabled old people in London face a bleak future.

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SIR,—Your Dec 14 editorial assumes that private nursing homes will have an essential future role in the care of old people. Lower costs are stated as one advantage yet no account is made of the cost of care by the primary health care team. A private nursing home increases the number of old people in an area and this may play havoc with the long-term planning of services for the elderly and