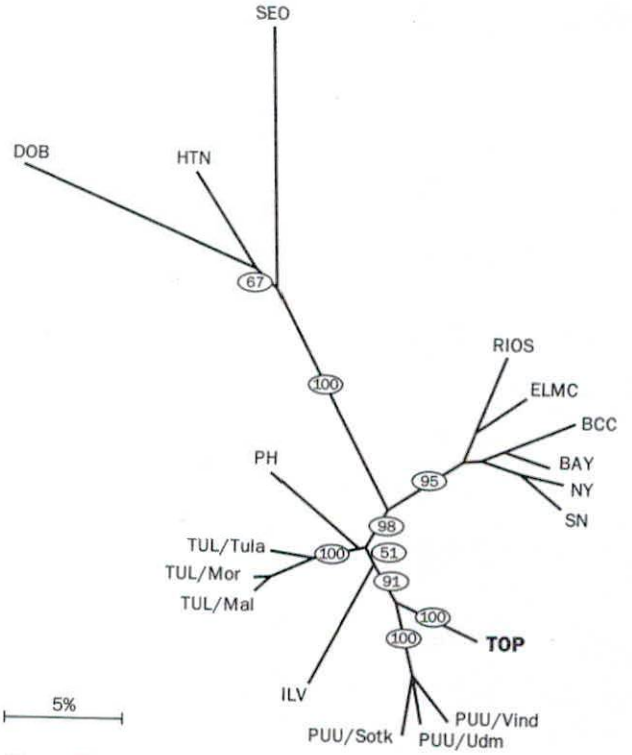

Figure: **Phylogenetic tree illustrating position of Topografov virus**

Best Fitch-Margoliash tree generated for nt 29–333 of the TOP S-segment encoding nucleocapsid protein (sequences of the amplification primers excluded). Branch lengths are proportional to genetic distances. The bootstrap support percentages of particular branching points calculated from 500 replicates are given in ovals. For comparison, existing sequence data were obtained from the Genome Sequence Database. HTN=Hantaan virus, strain 76118 (Gene Bank accession number M146271); SEO=Seoul virus, strain SR-11 (M34882); DOB=Dobrava virus (L41916); PH=Prospect Hill virus, strain PH-1 (Z49098); TUL=Tula virus, strains Tula/76Ma/87 (Z30941), Moravia/5286Ma/94 (Z48573) and Malacky/Ma32/94 (Z48235); ILV=Isla vista virus, strain MC-SB-1 (U31534); PUU=Puumala virus, strains Sotkamo (X61035); Vindeln/83-L20 (Z48586) and Udmurtia/458g/88 (Z30707); RIOS=Rio Segundo virus, strain RMx-Costa-1 (U18100); ELMC=El Moro Canyon virus, strain RM-97 (u11427); BAY=Bayou virus, strain Louisiana (L36929); BCC=Black Creek Canal virus (L39949); SN=Sin Nombre virus, strain H10 (L25784); NY=New York virus, strain RI-1 (U09488).

represent a previously unknown hantavirus genotype (figure). We name the virus Topografov (TOP) after its origin, the area around the Topografov river.

TOP comprises a separate lineage on the phylogenetic tree which is situated within the group of hantaviruses carried by *Arvicolinae* rodents: Puumala, Tula, Prospect Hill, and Isla Vista, and shows from 76 to 78% identity with their S-segment sequences. Sin Nombre, New York, Bayou, Black Creek Canal, El Moro Canyon, and Rio Segundo hantaviruses carried by *Sigmodontinae* rodents in the USA are less related to TOP (70–73%) and Hantaan, Dobrava, and Seoul hantaviruses carried by *Murinae* rodents show the least similarity (54–57%). As *Lemmus* belong to the *Arvicolinae* subfamily of the *Muridae* family, our data are consistent with the concept that phylogenetic relationships between hantaviruses resemble those of their natural hosts.[1,2] Preliminary results on characterisation of the TOP nucleocapsid protein, using panels of monoclonal antibodies prepared against Puumala and Tula viruses, show that it is antigenically distinct from other hantaviruses carried by *Arvicolinae* rodents.

Mass movements of Norwegian lemmings during outbreak years are well-known in Fennoscandia.[3] In the traditions of many northern people, there are references to dise transmitted by lemmings (lemming fever). One s lemming year, 1942, coincided with epidemics of hund of cases of fever with renal manifestations and occasio myopia in German and Finnish troops stationed in Lapl Whether these epidemics were due to Puumala or TOP and whether this phylogenetically old virus is pathog remains to be solved. Notably, from all hantaviruses ca by *Arvicolinae* rodents, only the European Puumala viru known to be pathogenic, so far, in human beings.

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1 Nichol ST, Spiropoulou CF, Morzunov S, et al. Genetic identificati of a hantavirus associated with an outbreak of acute respiratory illnes *Science* 1993; **262:** 914–17.

2 Plyusnin A, Vapalahti O, Lankinen H, et al. Tula virus: a newly detected hantavirus carried by European common voles. *J Virol* 199 **68:** 7833–38.

3 Stenseth NC, Ims RA (eds). The biology of lemmings. *Linnean Soc Symp Series* 1993: 15.

4 Miasnikov YA, Apekina NS, Zuevski AP, et al. [The disposition of natural foci of hemorrhagic fever with renal syndrome in different landscape areas of Tyumen Province]. *Vopr Virusol* 1992; **37:** 161–65 (in Russian).

5 Hortling H. En epidemi av fältfeber (?) i finska Lappland. *Nord Med* 1944; **30:** 1001–04.

Blood-based PCR assay to detect pulmonary tuberculosis

SIR—Condos and colleagues (April 20, p 1082)[1] report that PCR testing of blood samples in patients with suspecte pulmonary tuberculosis had a very high overall sensitivi (95%). This sensitivity compares very favourably with resul obtained by conventional methods such as sputu microscopy, and it is quite similar to that obtained with PC of sputum samples.

We have reported that *Mycobacterium tuberculosis* DN could be detected in some patients with pulmona tuberculosis.[2] In a more recent prospective protocol w evaluated the effectiveness of blood-based PCR assay for th diagnosis and follow-up of 19 patients (6 HIV-positive an 13 HIV-negative) with sputum-smear positive and culture proven pulmonary tuberculosis, and in 18 patients withou tuberculosis who served as a control group. PCR was done as before,[3] with minor modifications. Samples were obtained a diagnosis and at 1, 3, 6, 9, and 12 months later. By contras with the sensitivity of 95% communicated by Condos and colleagues, blood PCR was positive in only eight of 19 patients (42%), although the specificity of PCR in blood wa similar among HIV-positive (2/6, 33%) and HIV-negative patients (6/13, 46%). Only 17% of our patients had positive blood cultures for *M tuberculosis*. Of note was that DNA of *M tuberculosis* could not be detected at the moment of diagnosis in five patients, but PCR became positive in all of them after start of treatment. The PCR test continued to be positive in eight patients at 1 month of therapy, in two at 3 months, and in one at 9 months. The clinical course of all our patients was favourable and not linked to the result of blood PCR.

Our results are not as supportive of a role for blood PCR in the diagnosis of pulmonary tuberculosis as the data reported by Condos and colleagues, whose results are surprising when taking into account the fact that blood-based PCR detection of *M tuberculosis* is often cumbersome because of the frequent

esence of inhibitors in the sample.[2] By contrast with our tudy, only 37% of their patients with pulmonary berculosis were sputum-smear positive, and less than 4% n comparison with 17% in our series) had ycobacteraemia, which could reflect a low bacterial burden n a majority of them, and this makes it difficult to derstand the enormous (95%) sensitivity of blood PCR. nally, it would be useful to know whether they found any discrepancy in their results when the samples of PCR positive patients were processed in duplicate.

If Condos and colleagues' data are confirmed by other groups, many concepts in the pulmonary tuberculosis will need to be re-written, and blood-based PCR would then serve as an efficient substitute for conventional microbiological methods based in the study of sputum for the diagnosis of pulmonary tuberculosis.

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1 Condos R, McClune A, Rom WN, Schluger NW. Peripheral-blood based PCR assay to identify patients with active pulmonary tuberculosis. *Lancet* 1996; **347:** 1082–85.
2 Folgueira L, Delagado R, Palenque E, Aguado JM, Noriega AR. Rapid diagnosis of *Mycobacterium tuberculosis* bacteremia by PCR. *J Clin Microbiol* 1996; **34:** 512–15.
3 Folgueira L, Delagado R, Palenque E, Noriega AR. Detection of *Mycobacterium tuberculosis* DNA in clinical samples by using a simple lysis method and polymerase chain reaction. *J Clin Microbiol* 1993; **31:** 1019–21.

Multidrug resistant tuberculosis in South Africa

SIR—Nkqubela Chest Hospital in the Eastern Cape province of South Africa, admits over 2000 patients with tuberculosis (TB) annually. Short course chemotherapy including rifampicin has been standard treatment since 1980. The multidrug resistance (MDR) rate is low and does not change significantly from year to year.

	July-Dec 1993	1994	1995
Sensitive to all drugs	331	657	629
Resistant to INH and rifampicin	7 (2·1%)	14 (2·1%)	14 (2·2%)
Resistant to INH	39 (11·8%)	63 (9·6%)	54 (8·5%)

During 1995, two resistant patients were admitted after failed treatment at other centres. All the others started treatment at Nkqubela, had no history of previous treatment, and were therefore resistant at their first admission. None were known to be HIV seropositive; routine testing is not undertaken, but none had evidence of HIV infection.

The absconding rate at Nkqubela averages 7·8%; it is actually lower, because a few patients abscond repeatedly. They are admitted sick, leave when they feel better and return when they relapse. Not one of these has developed resistant organisms; not even one who has been admitted 8 times in less than 3 years. No MDR patient has a relative or contact with MDR TB. The report of an MDR infection arrives 3 months or more after admission. No incident of crossinfection has been recorded, even among HIV seropositive contacts.

TB clinics in a group of refugee camps in Somalia in 1986–89 recorded an incidence of 0·7% of failed treatment in patients initially sputum positive—ie, still sputum positive after 6 months of chemotherapy. The default rate was 17·8% over one year. Many patients had previous treatment in other camps, but they rarely admitted it. There was no HIV infection in Somalia at the time. Recreational drug consumption in Somalia was limited to harmless Xat. In the Eastern Cape, alcohol and marijuana are popular but there is no intravenous drug culture in either environment. At Nkqubela the incidence of HIV infection is unknown, since patients often refuse to be tested.

In neither of these two very different environments does drug resistance seem to have any relationship to erratic or previous treatment. All the evidence suggests that the resistance or sensitivity of the infecting organism is defined before treatment begins, does not alter thereafter, and is not altered subsequently by HIV infection or repeated treatment.

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HHV8 DNA in angiolymphoid hyperplasia of the skin

SIR—We have reported Kaposi's sarcoma-associated HHV8 DNA sequences in an angiosarcoma of the face in an HIV-negative patient, suggesting that this virus may be implicated in the pathogenesis of an endothelial cell-derived cancer other than Kaposi's sarcoma (KS).[1] Benign angiogenic lesions, on the other hand, have been found not to contain HHV8 sequences.[2,3] We report four cases of HHV8 sequences in patients with angiolymphoid hyperplasia and eosinophilia (ALHE).

DNA was extracted from the paraffin-embedded tissue specimens of four patients with histologically confirmed diagnosis of ALHE. All patients were HIV-negative and had no clinical signs of immunodeficiency. PCR with primers specific for the 233 bp $KS330_{233}$ fragment was carried out as described by Chang et al.[2] We detected 233-bp bands in each of the four ALHE lesions. The specificity of the bands were confirmed by hybridisation to a previously sequenced HHV8 probe obtained from KS tissue.[3]

ALHE is an uncommon benign disorder characterised by soft angiomatous tumours usually on the face, ear, or scalp.[4] The main histological feature is proliferation of atypical endothelial cells (as seen in KS and angiosarcoma of the face) accompanied by an infiltrate of eosinophils and lymphocytes. Vascular tumours characterised by the proliferation of atypical epitheloid endothelial cells with abundant eosinophilic hyaline cytoplasm span a broad spectrum of histological appearances and behaviour. At the benign end are the epitheloid haemangiomas such as ALHE and at the malignant end are highly aggressive epitheloid angiosarcomas. The presence of HHV8 sequences in both benign and malignant proliferations of endothelial cells suggests that the virus alone is not sufficient to produce a specific lesion.

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1 Gyulai R, Kemény L, Kiss M, et al. Herpesvirus-like nucleic acid sequence in angiosarcoma in a patient without HIV infection. *N Engl J Med* 1996; **334:** 540–41.
2 Chang Y, Cesarman F, Pessin MS, et al. Identification of new human herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. *Science* 1994; **266:** 1865–69.
3 Kemény L, Gyulai R, Kiss M, et al. Herpesvirus-like nucleic acid sequences in patients with Eastern European sporadic Kaposi's sarcoma. *J Invest Dermatol* 1996; **106:** 381.
4 Olsen TG, Helwig EB. Angiolymphoid hyperplasia with eosinophilia. *J Am Acad Dermatol* 1985; **12:** 781–96.