This would suggest a score of two out of two against universities as upholders of intellectual standards of honesty. It leaves the victim of such theft very much in the cold.

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Storage of information by medical journals

SIR,—Like you in your Nov 17 editorial "Brevity in *The Lancet*" we decided to "store, rather than print, the fine detail" of certain articles which we call, in their published form, Technical Briefs. We have published 5–10 in each monthly issue since 1986.

We have been surprised at the rarity of requests for these stored details: among several hundred Technical Briefs published so far, we have received only one such request. Of course, we do not know the frequency with which authors are contacted directly by interested readers.

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DAVID E. BRUNS,
Editor

Placental localisation in early pregnancy

SIR,—I disagree with the statement in your Feb 2 editorial that "placental localisation at the initial scan cannot be recommended, and when a low placenta is noted incidentally, it is not necessary routinely to order a third-trimester scan".

Having been in practice as an obstetrician gynaecologist, and specialising solely in prenatal diagnosis for the past 10 years, it is my experience that the advent of new equipment certainly results in better visualisation for sonograms done in the first and early second trimester, especially with respect to the high instance of diagnosis of low-lying placenta. I believe that the term placenta praevia is inappropriate before 12 weeks' gestation, unless placental tissue can be clearly seen to cover the internal os region. It is regarded as routine to always visualise the internal os and the whole endocervical canal with an empty bladder to prevent any anatomical distortions. Central placenta praevia can be diagnosed in early pregnancy, especially when the relation of the placental tissue to the os and the endocervical canal is noted. In my experience with these cases, usually without any further abnormal bleeding, repeat sonography between 16 and 18 weeks' or as late as 20 weeks' gestation, allows further confirmation of persistent praevia.

Prenatal diagnosis is routinely recommended for all women aged 35, when the incidence of chromosome abnormalities is 1%. Surely central placenta praevia with a population frequency of less than 1% or a delivery frequency of placenta praevia, which you cite as anything from 2·3% to 16·9%, warrants a routine repeat sonogram when in early pregnancy the placenta is seen to be overlying the os?

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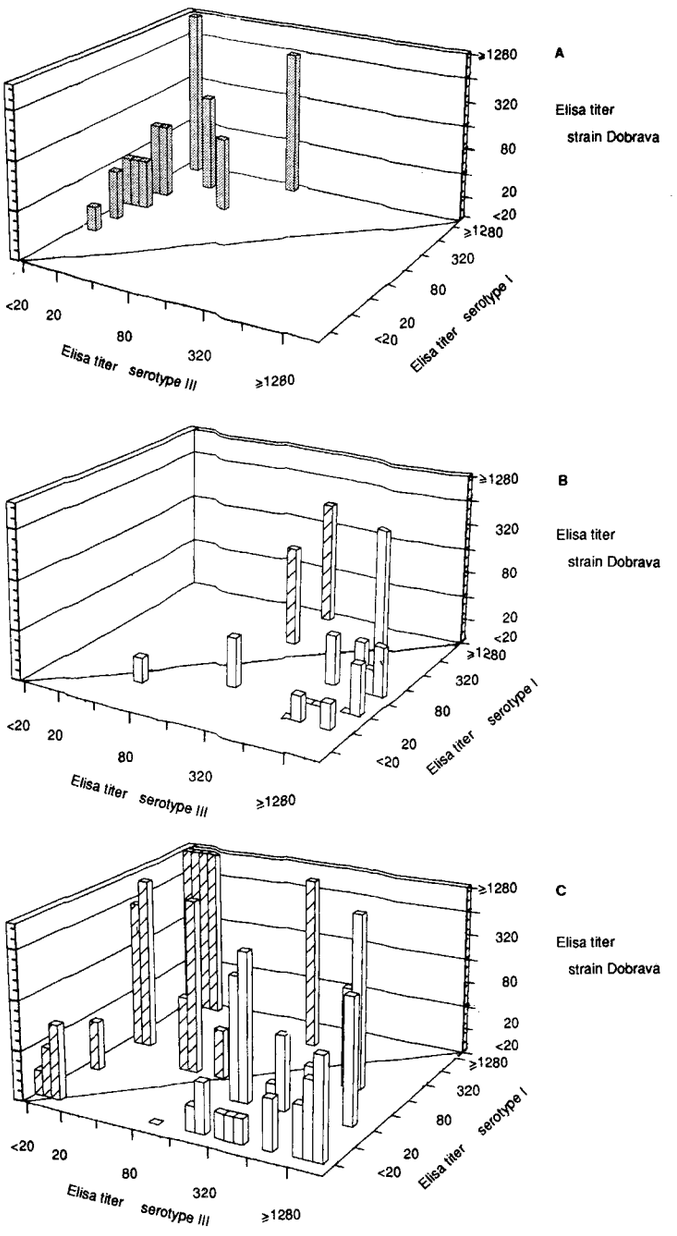
Different hantavirus serotypes in western Europe

SIR,—So far, human infections with hantavirus, causing haemorrhagic fever with renal syndrome (HFRS), other than those transmitted by laboratory animals, have in western Europe been associated with serotype III.[1,2] The main reservoir host is the red bank vole *Clethrionomys glareolus*. In the Netherlands we have found serological evidence for serotype III in people who were probably infected via contact with wild rodents.[3] We have now demonstrated this virus in animals. In lung extracts of four seropositive red bank voles caught in an area of the Netherlands where eight confirmed human cases of HFRS had been documented, viral antigen was identified by ELISA. The ELISA identified the virus as serotype III.[2]



Antibody titres of human sera in ELISA, measured against hantavirus serotype I, serotype III, and strain Dobrava.

(A) 11 sera from laboratory-associated cases and (B) 16 sera from non-laboratory-associated cases in Netherlands and Belgium; and (C) 32 sera from non-laboratory-associated cases in Yugoslavia.

With the same ELISA system we have tested 32 immunofluorescent antibody positive sera, collected from people with a non-laboratory-associated infection in Yugoslavia, against serotype I (strain HV 76-118) which strongly cross-reacts with serotype II (SR-11),[2] serotype III (Hällnäs), and a recent isolate from Yugoslavia (strain Dobrava).[4] The Dobrava strain was isolated from the yellow-necked field mouse (*Apodemus flavicollis*) during a recent period of high incidence of HFRS in Yugoslavia;[4] it reacted more strongly with sera specific for serotypes I and II than with sera specific for serotype III. In addition 16 positive sera from non-laboratory-associated infections and 11 positive sera from laboratory-associated infections in the Netherlands and Belgium were tested in the ELISA against these three viruses. All sera from the laboratory-associated infections showed higher titres against serotype I and strain Dobrava than against serotype III (figure, A). The titres of these sera against serotype I were slightly higher than those against strain Dobrava. All but 2 of the 16 sera from non-laboratory-associated infections in the Netherlands and Belgium showed the highest titres against hantavirus serotype III (figure, B). 14 of the 32 sera from Yugoslavia showed the highest titres against serotype I and strain Dobrava, whereas the other 18 reacted more strongly against serotype III (figure, C). This confirms the results of an earlier serological study with an IFA,

which indicated that two different hantavirus serotypes caused HFRS in Yugoslavia.[5]

1 serum from the Netherlands and 1 from Belgium reacted more strongly with serotype I and strain Dobrava than with serotype III. Furthermore, both sera neutralised serotype I (strain HV 76-118) in an 80% plaque reduction neutralisation assay, with titres of 10 and 40, respectively (Jim LeDuc, USAMRIID, Frederick, USA, personal communication). Both individuals had recently been infected and had not recently been abroad. In a report by Pilaski and co-workers, 1 out of 21 sera from HFRS patients in Germany proved to react more strongly with serotype I.[6] These data suggest that in western Europe as in Yugoslavia non-laboratory-associated hantavirus infections may be caused by more than one serotype.

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Increasing incidence of resistance among shigellae to trimethoprim

SIR,—Shigella organisms resistant to trimethoprim (TMP) and other antimicrobial agents have been reported,[1,2] and this had led to re-evaluation of the treatment regimen for shigellosis.

The first report of TMP-resistant shigellae in Ontario, Canada, appeared in 1980.[3] Examination of isolates between 1977 and 1979 revealed 3% resistance to TMP among *S sonnei* and *S flexneri* 2A strains. As part of a long-term follow-up study of TMP resistance among *Shigella* spp all isolates from stool samples received in our diagnostic enteric laboratory at the Central Public Health Laboratory, Ontario, Canada, between January and December, 1990, were examined for susceptibility to TMP and sulphamethoxazole (SMX). Susceptibility was determined by the agar dilution method with a Steers multiple replicator apparatus.[4]

Our results showed an increase in TMP resistance among *S sonnei* isolates (12%) and a striking increase among strains of *S flexneri*—21% and 9% for *S flexneri* 2A and 3A, respectively. TMP resistance, not encountered in the previous study,[3] was found among *S dysenteriae* type 1 strains; 6% of isolates were resistant. All strains were highly resistant with minimum inhibitory concentration (MIC) greater than 1000 μg/ml. All isolates also showed concomitant resistance to SMX with MIC above 512 μg/ml, and resistance to co-trimoxazole (TMP/SMX combination) with MIC more than 4/76 μg/ml.

We were able to transfer resistance to both TMP and SMX from all shigella isolates to *Escherichia coli* K-12 strain 711. The MICs of TMP and SMX in the *E coli* transconjugants were much the same (greater than 1000 μg/ml and 512 μg/ml, respectively) as those for the shigella isolates. None of the isolates were resistant to the fluoroquinolones ciprofloxacin and norfloxacin, which had MICs of less than 1 μg/ml and less than 4 μg/ml, respectively.

The finding that a high percentage of strains in this study transferred resistance to TMP and SMX emphasises the potential for dissemination of these resistance factors to other strains. The pattern observed also shows the need for prudent use of antimicrobial agents in the treatment of shigellosis.

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Heparin and inflammatory bowel disease

SIR,—Mr Gaffney and colleagues (Jan 26, p 238) show a clinical response to heparin in 3 patients with inflammatory bowel disease. As they comment, thromboembolic complications are a recognised feature of inflammatory bowel disease.[1] I have managed 1 patient with Crohn's colitis and 2 with ulcerative colitis in whom venous thrombosis and pulmonary emboli developed in conjunction with active bowel disease, and none of whom improved while on heparin.

A 27-year-old man with a severe exacerbation of Crohn's colitis had an ileofemoral vein thrombisis complicated by multiple pulmonary emboli. He was treated with intravenous heparin 40–50 000 U/day for one month in conjunction with systemic corticosteroids and enteral nutrition, but despite this treatment his condition deteriorated and he underwent colectomy.

I also question the wisdom of taking multiple endoscopic biopsy specimens from patients on anticoagulants. The occlusive fibrinoid ateriolar lesions reported in Crohn's disease could be a consequence of the inflammatory response rather than its cause.[2]

The history of inflammatory bowel disease is punctuated by case reports of potential promising treatments. However, what is needed are large controlled clinical trials to evaluate the efficacy of new and established treatments. Despite the high prevalence of Crohn's disease and ulcerative colitis in Western countries such studies are sadly lacking. Cardiologists have set the standard for clinical trials in the 1990s that gastroenterologists should follow.

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Codon 178 mutation in ethnically diverse Creutzfeldt-Jakob disease families

SIR,—We recently described a GAC-to-AAC mutation in codon 178 of the amyloid precursor gene in a Finnish family with Creutzfeldt-Jakob disease (CJD).[1] We now report that this same mutation, which results in a substitution of asparagine for aspartic acid in the encoded protein, is linked to transmissible CJD in American families of Dutch and Hungarian descent, and in a French family from Brittany.

The Dutch-American pedigree (family B in May and colleagues' description,[2] family MD in a review by Masters et al[3]) currently includes 10 cases in three generations, 2 with transmission of disease to non-human primates. The Hungarian-American kindred (ST[3]) now has 9 affected members in four generations, with 2 instances of transmission. The French kindred (AB) has 3 affected members in two generations, and 1 transmission. These patients have had comparatively early onset of disease (mean 47 years, range 35–63) and long duration of illness (mean 14 months, range 6–36); however, they showed a characteristically broad array of clinical manifestations, including dementia, signs of cerebellar, visual, and