deficiency, or improving it, as with the α thalassaemia traits.[6]

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Tuberculosis and HIV infection

SIR,—When analysing the results of three large clinicoepidemiological studies (including that of Dr Kevin M De Cock and colleagues) on HIV seropositivity in patients with tuberculosis in Africa,[1-3] one cannot fail to notice that patients with presumed pulmonary tuberculosis are more likely to be positive for HIV than patients with bacteriologically proved tuberculosis (table). In one study the excess was significant.[3]

Unfortunately, the clinical case definition for presumed pulmonary tuberculosis used in these reports was far from uniform. In the Ivory Coast presumed pulmonary tuberculosis was defined as including patients with "consistent clinical and radiological features but whose sputum smears gave negative results."[1] In Zambia it was defined as occurring in "a patient attending a chest clinic and treated for TB not confirmed by sputum smear or culture" with (suggestive?) "clinical and radiological findings."[2] In the Zairean study the definition included "clinical symptoms, and radiological signs showing alveolar infiltrates with or without cavitation but no bacteriological proof"; the infiltrates also "had to be resistant to common antibiotics."[3] All these clinical case definitions lack specific diagnostic criteria. This leaves a few questions to be answered. How many of those patients with presumed pulmonary tuberculosis really had pulmonary tuberculosis? What is the positive predictive value for tuberculosis of the above case definitions? How could the investigators reliably differentiate pulmonary tuberculosis from the many other diseases associated with HIV that affect the lower respiratory tract[4,5] without the help of additional investigations and culture facilities?

Recently we tried to address these questions by performing bronchoalveolar lavage and transbronchial biopsy in 92 HIV positive patients with fever, weight loss, and chronic cough but negative results of sputum smear for acid fast bacilli and pulmonary infiltrates not clearing with standard antibiotic treatment. Pulmonary tuberculosis was confirmed in only 17 cases, while in 68 patients another pulmonary disease associated with HIV was shown (unpublished data). Among 23 patients with alveolar infiltrates in chest *x* ray films, pulmonary tuberculosis was confirmed in only six. Although our findings may not be extrapolated as such to other African countries, these data suggest that the above clinical case definitions of presumed pulmonary tuberculosis are too imprecise.

We are aware that bronchoalveolar lavage and transbronchial biopsy are cumbersome procedures not widely available in Africa. Equipment and logistic support should be provided to reference hospitals to carry out these procedures. Meanwhile, we propose a more stringent working case definition for presumed pulmonary tuberculosis: a patient with repeatedly negative sputum smears for acid fast bacilli, fever, weight loss, persistent cough for more than one month, pulmonary infiltrates (all types) in chest *x* ray films, not resolving with the usual antibiotics but clearly improving within eight weeks of treatment for tuberculosis.

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Prevalence of HIV in patients with pulmonary tuberculosis in Africa

Site of study	No (%) of patients with confirmed pulmonary tuberculosis positive for HIV	No (%) of patients with presumed pulmonary tuberculosis positive for HIV	p Value
Abidjan, Ivory Coast[1]	609 (38) (n=1610)	53 (44) (n=120)	0·16
Lusaka, Zambia[2]	73 (49) (n=149)	60 (59) (n=101)	0·10
Kinshasa, Zaire[3]	94 (33) (n=287)	60 (45) (n=132)	<0·02

Vitamins and IQ

SIR,—Mr Stephen Schoenthaler,[1] in his response to Mr Richard Peto,[2] repeats the claim made in his original paper[3] that the improvements in IQ seen in the children given supplements "were concentrated in approximately one third of the sample," implying that they were a subgroup deficient in vitamins and minerals. A more correct analysis of the data obtained with the Wechsler intelligence scale for children—revised (WISC-R)—shows that this claim is unfounded. In addition, even if it was tenable, the assumption that the group was at risk nutritionally is highly unlikely.

Mr Schoenthaler's table[1] gives the means and standard deviations (SD) of the initial and final values obtained with the WISC-R in the four treatment groups, showing that the eight SDs all lie between 12·2 and 14·6 points in value. If the effect of the supplement was to increase IQ in just some children but to leave others unaffected this would inevitably increase the SD of the IQ distribution in the groups given supplements. There is no evidence of this at all in the table. Moreover, using the data from table 5 of the original paper,[3] the SDs of the *increase* in IQ in the four treatment groups (ranging from 7·3 to 8·9 points) are insignificantly different from each other. This confirms that the increase in IQ seen in the group given 100% supplements is no more variable than would occur by chance. Thus it is a whole group, not a subgroup, response.

It is hard to believe that a vitamin and mineral supplement affecting the IQ of the whole group exerts its action by correcting nutritional deficiency as most of the group is likely to be nutritionally fit. Furthermore, as Schoenthaler *et al* point out, the "improvements [in IQ] occurred in all the schools sampled."[4] Of the four schools studied, Riverbank is in an economically depressed area in which a substantial proportion of the residents receive public assistance, while Oakdale contains students from among the most expensive homes in the county, with nearly half of them having IQs over 120. The suggestion that these two samples of students should have similar rates of vitamin deficiency is clearly unlikely.

The conclusion, taking into account the non-linear relation between the amount of supplement and the improvement in IQ,[4] is that the findings are not compatible with a nutritional explanation.

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SIR,—The letters of Dr David Benton[1] and Mr Stephen Schoenthaler[2] give the impression that several studies have reported a consistent effect of vitamin supplementation on IQ. In fact, there are incongruities among the findings of the studies that they claim are consistent, and their authors are inconsistent in their interpretations of them.

Dr Benton's initial Welsh study[3] found an effect of supplementation among all children, but in his subsequent Belgian study the effect was limited to those who had a poor diet and even then was seen only among boys.[4] The comment was made that because the Welsh children had a much better diet than the Belgian children they should not have benefited from supplementation.[5] In response Dr Benton suggested that the Welsh findings were "atypical" and stated that "there is no general effect [of supplementation] on non-verbal reasoning."[6]

A major criticism of the study of Schoenthaler *et al*[7] concerned multiple significance testing.[8,9] Mr Schoenthaler responded that he "correctly predicted that among the four cohorts the 100% formula should produce the best results."[2] This is in conflict with the statement in the paper that "no predictions were made at the beginning of the experiment concerning the supplementation which would give optimal results."[7] There is also conflict between reports of his interpretations of the findings. In the original paper Schoenthaler *et al* state that there is "one firm conclusion . . . about cognitive effects of dietary supplementation . . . there are such effects, they act in a predictable manner and they occur in children who would be considered as receiving a sufficient diet."[7] In response to a critical editorial,[10] however, he stated that "until our study is properly replicated, it [the effect of supplementation] appears tentative."[11]

The inconsistencies in the statements of Dr Benton and Mr Schoenthaler raise doubts about the interpretation to be placed on their findings. The issue of the effect of vitamin supplementation on IQ is not resolved. A large and well conducted clinical trial is still required.

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Estimations of gestational age and screening for Down's syndrome

SIR,—Mr S Holding reports the problems that inaccurate estimation of gestation causes in screening for Down's syndrome.[1] We have also experienced this problem but approached its solution from a different direction.

The table shows risks of Down's syndrome calculated using previously reported variables for weeks 15-18 of gestation for four randomly selected patients screened at the Royal Gwent Hospital.[2-4] Risks are based on measurements of α fetoprotein and human chorionic gonadotrophin concentrations in a single sample. Estimation of gestational age from the date of the last menstrual period in women who are sure of their dates may result in errors of greater than two weeks in 17% of women.[4] Examination of the risks in cases 1 and 2 shows that it is quite conceivable that referral for amniocentesis may be wrongly indicated or denied depending on the estimated gestational age. Similarly, gestational ages derived ultrasonically may be inaccurate by ±7 days,[5] which could also result in amniocentesis being indicated or denied wrongly.

We evaluated the use of the biparietal diameter measured on the day that blood sampling was done as an indicator of gestational age by regression analysis of biparietal diameter versus α fetoprotein or human chorionic gonadotrophin concentration (paper in preparation). This showed that risks calculated by week of gestation (defined by a size band for biparietal diameter—for example, 34·1-38·0 mm=16 weeks) are inadequate because at the extremes of the size band a 0·1 mm change in the measured biparietal diameter (resulting in a change of estimated week of gestation) may cause a 35-43% change in the calculated risk of Down's syndrome (based on two variables, α fetoprotein and human chorionic gonadotrophin concentration). If three variables are used the change may be as large as 150%. Furthermore, the imprecision in ultrasound measurement has been reported as up to 1·7 mm for a 51 mm object.[6] Thus errors in assignment of week of gestation are likely to be frequent.

Unfortunately, imprecision in assays of biochemical variables and in ultrasound measurement of biparietal diameter is unavoidable. The method for calculating the risk of Down's syndrome[3] inevitably results in amplification of these errors, and therefore every effort should be made to avoid adding extra imprecision. We therefore propose that instead of using the relatively inaccurate estimates of gestation obtained by calculation from the date of the last menstrual period or from size banded biparietal diameter, the measured biparietal diameter should be used as the most accurate indicator of gestational age currently available.

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Bilateral diaphragmatic paralysis may be misdiagnosed as pulmonary embolism

SIR,—Dr A Nisbet and colleagues' lesson of the week purports to describe a case of bilateral diaphragmatic paralysis with apparent radiological evidence of pulmonary embolism.[1] Analysis of the radiographic findings and findings on isotope lung scanning, however, does not suggest pulmonary embolism. They describe bilateral basal perfusion defects and evidence of bilateral basal plate atelectasis on radiography. This is thus an indeterminate perfusion scan, which neither supports nor excludes the diagnosis of pulmonary embolism. The authors state that the ventilation scan was normal. That may be so, but in the presence of radiographic abnormalities such a scan must be regarded as a false negative scan. The reason for a false negative ventilation scan may be either poor spatial resolution or that the images were obtained in an inappropriate projection.

In other words, unmatched ventilation-perfusion defects should not be regarded as indicating a high probability of pulmonary embolism when the perfusion defects are matched by radiographic abnormalities. This simply reflects the insensitivity of ventilation scanning. When the perfusion defects match radiographic abnormalities the scan is indeterminate and pulmonary angiography is required to confirm or exclude pulmonary embolism.

The conclusion that the radiological signs of bilateral diaphragmatic paralysis mimic those of pulmonary embolism is thus not sustainable. Indeed, why should the signs of diaphragmatic paralysis mimic those of embolism? Surely diminished ventilation in the lower zones would be expected to be the initial abnormality when the diaphragms are paralysed, whereas hypoperfusion is obviously the underlying abnormality in embolism.

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AUTHOR'S REPLY,—Plate atelectasis is well described in pulmonary embolism and also in bilateral diaphragmatic paralysis. Physicians are more likely to encounter pulmonary emboli than diaphragmatic paralysis and, therefore, bilateral diaphragmatic weakness is often misdiagnosed as pulmonary embolism. We agree that the ventilation-perfusion lung scan was difficult to interpret and this is not an uncommon problem. Pulmonary angiography is not, however, needed when the physician is aware of the clinical signs of bilateral diaphragmatic weakness.

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Preventing the spread of HIV infection

SIR,—Dr P D French and colleagues[1] describe trends in cases of gonorrhoea among homosexual men attending two sexually transmitted diseases clinics in London that are remarkably consistent with those reported recently from diverse geographical locations.[2-5] A period of decline reached a minimum in 1988 and was followed by an increase in both 1989 and 1990. The recent upturn has been interpreted by some workers as evidence for a parallel increase in the frequency of sexual acts that might permit the transmission of HIV. Dr French and colleagues[1] and Tomlinson *et al*[6] have questioned this interpretation on the grounds of the different patterns of infectivity of the gonococcus and HIV.

Waugh talked of a "return to unsafe sexual practices,"[4] and van den Hoek *et al* talked of a "relapse into high risk sexual behaviour."[3] The impression created is that a group of homosexual men, having made changes towards safer sexual practices, are reverting to their previous unsafe practices. To assess whether this impression is justified we compiled data on homosexual men with gonorrhoea attending the Praed Street Clinic at St Mary's Hospital, Paddington, during the first two weeks of February, May, August, and November during 1985-8. The table gives the median age and range of ages of these men.

Median age and range of ages of homosexual men with gonorrhoea presenting to clinic during first two weeks of February, May, August, and November during 1985-8

	No of men	Median age	Age range
1985	23	29	21-55
1986	26	31	20-53
1987	4	27	23-39
1988	13	30	19-52

The median age of the men attending does not seem to be increasing. It seems improbable that diagnoses of gonorrhoea reported from sexually transmitted diseases clinics over several years represent cases incident in the same cohort. Probably many of the cases diagnosed towards the end of a period will occur among people who have become more sexually active since the beginning of the period. In this case the reported upturn in cases of gonorrhoea suggests that the priority for prevention programmes might be to get the message about safer sexual practices across to younger people who are becoming more sexually

Risk of Down's syndrome (gestation weeks 15-18) based on α fetoprotein and human chorionic gonadotrophin concentrations in single sample calculated for four randomly selected patients

Case No	Mother's age at estimated date of delivery (years)	α Fetoprotein (kU/l)	Human chorionic gonadotrophin (U/ml)	Risk by week of gestation			
				15	16	17	18
1	28·9	67	49	2250	1362	401	290
2	33·5	14	23	491	301	125	86
3	32·4	21	9	4063	2539	1147	757
4	20·3	20	19	3226	1941	859	567