refuse this we give 2 mg phytomenadione (vitamin K₁) orally at birth and at 12 and 24 hours of age. We await information on the efficacy of this oral regimen. Recent work by Cornelissen *et al* will further fuel the controversy as they suggest that a single dose of vitamin K, whether given orally or intramuscularly, is insufficient to protect against late haemorrhagic disease of the newborn.⁶ I wonder whether, in the meantime, the adverse publicity surrounding vitamin K will result in a resurgence of this preventable condition; I hope that it remains a condition that is rarely seen.

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Antenatal screening for Down's syndrome

EDITOR,—In maternal serum screening for Down's syndrome based on several markers the human chorionic gonadotrophin assay can measure either the intact molecule or the free β subunit (a small fraction of the total), or both. Kevin Spencer advocates using an assay of the free β subunit,¹ and, though N J Wald and colleagues are uncertain,² we believe that there are two good reasons to prefer the free β subunit.

Firstly, when screening takes place—generally at 15-20 weeks' gestation—the predicted detection rate is higher for the free β subunit. In meta-analysis of 17 studies that used intact or total human chorionic gonadotrophin the average level for 530 Down's syndrome pregnancies was 2.0 multiples of the normal gestation specific median (95% confidence interval 1.9 to 2.1).³ When this approach is applied to the five reported studies that used free β (the four cited by Spencer² and that of Ryall *et al*⁴) the average level for 228 affected pregnancies is 2.3 multiples of the median (2.1 to 2.5).

The table shows the predicted effect of the

Detection rate and false positive rate (percentages) obtained in screening for Down's syndrome pregnancies with maternal serum α fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin (free β , intact or total) concentrations*

Cut off risk†	Human chorionic gonadotrophin			
	Free β		Intact or total	
	Detection rate	False positive rate	Detection rate	False positive rate
1 in 150	61	2.9	49	2.4
1 in 200	66	4.0	54	3.3
1 in 250	69	5.0	58	4.4
1 in 300	72	5.9	60	5.4
1 in 350	74	6.8	63	6.4

*Rates predicted from multivariate gaussian model with medians, standard deviations, and correlation coefficients of Spencer *et al*¹ and maternal age distribution of England and Wales in 1989 and 1990.
†Result of screening is positive if risk of Down's syndrome term pregnancy exceeds cut off.

increase in levels when screening using human chorionic gonadotrophin in combination with α fetoprotein and unconjugated oestriol. For the tabulated cut offs the predicted detection rate is 11-12% higher for free β , with a 0.4-0.7% increase in the false positive rate. For a fixed false positive rate there is an 8-10% higher predicted detection rate for free β . Possibly some of the increase in levels is an artefact of storage of the serum samples. This, however, is likely to be a small effect since the results of prospective screening at Oldchurch Hospital¹ are consistent with the model predictions: the detection rate is 73% (11/15) for a false positive rate of 5.5%.

The second reason for preferring the free β subunit is that, like α fetoprotein and unconjugated oestriol but unlike intact human chorionic gonadotrophin, it can be used for screening before 15 weeks. In the six published studies (three cited by Wald and colleagues² and three others⁵⁻⁷) of samples obtained in early pregnancy tested using intact or total human chorionic gonadotrophin the average level from 102 Down's syndrome pregnancies was only 1.2 multiples of the normal median. In contrast, in a recent study that used a free β assay at 7-13 weeks to test 13 affected pregnancies the average level was 1.85 multiples of the median, which is consistent with the average level after 15 weeks' gestation.⁸

These reasons have compelled us to change to assaying the free β subunit in our screening programme for Down's syndrome and to offer screening from 13 weeks' gestation. A disadvantage of screening for the syndrome before 15 weeks is that the α fetoprotein concentration cannot be interpreted in relation to neural tube defects. Many centres, however, would be confident enough in their use of routine ultrasound examination in screening for anomalies to abandon biochemical screening for this disorder in order to provide an earlier diagnosis of Down's syndrome.

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EDITOR,—Antenatal screening for Down's syndrome using maternal serum markers during the second trimester together with the woman's age is currently under investigation.¹ Haddow *et al* have reported the result of a large prospective study.² They showed the validity of predictions based on retrospective studies, indicating that use of the three markers α fetoprotein, chorionic gonadotrophin, and unconjugated oestriol is more effective than use of maternal serum α fetoprotein alone. Their results also suggested that not using

unconjugated oestriol values would lead to a 5% reduction in the rate of detection.

We conducted a prospective study using the two markers human chorionic gonadotrophin and unconjugated oestriol together with the woman's age. Such a protocol has been recommended for prenatal screening centres that do not measure α fetoprotein routinely to detect neural tube defects and are willing to use only two markers instead of three.³ We studied 26 128 women aged 18 to 37 who underwent prenatal screening for Down's syndrome between January 1990 and April 1992 in a limited area in north west France where the annual number of births is around 20 000. Gestational age was estimated by biparietal diameter ultrasonography before screening. Predictive risk factors were calculated by crossing hormone measurements with maternal age. Eligibility for amniocentesis or chorionic villus sampling was set up at a risk cut off of 1 in 150, leading to a positive screening rate of 4.7%. The risk factor calculation was based on published retrospective studies.^{4,5} Recent readjustment of reference values from our own study, however, indicated that risk factors had been overestimated and that our risk cut off was nearer 1 in 200.

Results of prospective study of prenatal screening for Down's syndrome based on human chorionic gonadotrophin and unconjugated oestriol concentrations and woman's age, according to second trimester risk cut off of 1 in 200

Maternal age (years)	No screened	Positive screening (%)	Cases of Down's syndrome		Detection rate (%)
			Detected	Not detected	
18-29	18 382	3.6	6	6	50
30-37	7 746	7.4	13	5	72
All ages	26 128	4.7	19	11	63

The table shows the effectiveness of our protocol. As expected, the detection rate was higher in the group of older women. We also observed that not using unconjugated oestriol values would lead to a net loss in detection of three cases (four cases missed and one additional case detected) for a similar positive screening rate (4.6%). Taken together with the data from Haddow *et al*, our results confirm the usefulness of measuring unconjugated oestriol concentrations—this had been questioned in a study by Macri *et al*.⁶

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1 Correspondence. Antenatal screening for Down's syndrome. *BMJ* 1992;305:768-71. (26 September.)
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EDITOR,—In our recent letter on antenatal screening for Down's syndrome we said that the effect of the age distribution of women on the performance of serum screening for Down's syndrome would be small and that, regardless of the variation in the age distribution, such screening would yield a higher

detection rate for a given false positive rate than screening using maternal age alone.¹

We examined the effect of the variation in the age distribution in different health districts in England and Wales in 1991.² To determine the effect at the extremes of the distribution we selected, firstly, the three districts with the highest proportion of births among women aged 35 or older (Richmond, Twickenham, and Roehampton; Hampstead; and Riverside), which in 1991 together had 19% of the births occurring among such women; and, secondly, the three districts with the lowest proportion of births among women aged 35 or older (Hartlepool; Barnsley; and Pontefract), which together had 5% of the births among such women.

The detection rate in the three districts with the highest proportion of births among older women would be, on average, 60% for a 5% false positive rate compared with 55% in the three districts with the lowest proportion for the same false positive rate. In England and Wales as a whole (with 9% of births among women aged 35 or more) the detection rate would be 58% for a false positive rate of 5%.

An important point that we did not make in our letter is that if the same risk cut off level was used there would be a notable difference in screening results between the two groups of districts. For example, with a risk cut off level of 1 in 250, the three districts with the highest proportion of pregnancies among older women would expect a 70% detection rate for a 9.0% false positive rate. In the three districts with the lowest proportion of pregnancies among older women the detection rate would be 52% for a 4.4% false positive rate. This represents the range of expected screening results. Roughly 90% of districts will have detection rates between 55% and 65%, with false positive rates between 5% and 8%. We would be pleased to supply the precise estimates for any particular district on request.

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Simulation model for planning renal services

EDITOR,—P G Bolger and R Davies use the Southmead renal programme to demonstrate a computer simulation model for renal services.¹ Unfortunately, we did not see their paper before publication. Had we done so we would have corrected some of the misleading information in it.

The paper uses information obtained in 1988-9 but presents it as current practice. The information in itself is inaccurate. The stated stock and acceptance rates on our renal programme for 1989, the starting point for simulation, are incorrect as they include children from a huge area not serviced by the adult unit. The distribution of new patients between haemodialysis and continuous ambulatory peritoneal dialysis is also incorrect: over the past three years the true ratio has been roughly the reverse of that quoted. The implication that haemodialysis is the preferred treatment, with continuous ambulatory peritoneal dialysis as the second choice if this is not possible, also misrepresents our practice. The stated upper limit for hospital haemodialysis is false, as at present there are some 70% more patients receiving this form of treatment than the quoted ceiling. The simulation also ignores the development of a full haemo-

dialysis and continuous ambulatory peritoneal dialysis service at the Gloucester Royal Hospital, which has greatly changed the population we serve.

The costs quoted were not validated by discussion with those of us working in the renal unit. They are inaccurate, especially as they contain no element for inpatient stays—relevant particularly to continuous ambulatory peritoneal dialysis and to some extent for the support of home haemodialysis. The costs for unit haemodialysis are overestimated. Thus it is not surprising that, based on the simulations for 1990-2000, the predicted pattern of our practice for 1992 is considerably different from what is actually happening, especially with regard to the costs.

The stated level of acceptance of new patients (40 per million population per year) is below our current practice and well below the accepted national need of 70-80 million population per year; this is recognised both by our purchasers and by us as providers. The purchasers have publicly announced their intention to increase investment in renal services and are working with us to increase treatment rates.

The computer model described may be excellent but is, of course, only as good as the data fed into it. The impression given in the paper of the practice, costs, and policies of Southmead Renal Unit is misleading. We are working with our purchasers to improve the quality, quantity, and efficiency of the service we provide. We do use a computer simulation program to help us with this; we have been careful to feed into it accurate information, but it is not the program that Bolger and Davies described.

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1 Bolger PG, Davies R. Simulation model for planning renal services in a district health authority. *BMJ* 1992;305:605-8. (12 September.)

AUTHOR'S REPLY,—We reported simulation runs using costs estimated in 1991, data collected in 1990, and assumptions about resource availability discussed with Southmead Renal Unit in 1989-90. The costs were obtained through the district finance department and were the best available at the time.

The purpose of our paper was to show what could be done with a simulation model, not to say anything specifically about Southmead. It was not our intention to present the work as reflecting the current practice of Southmead Renal Unit. We apologise to our colleagues at Southmead for any embarrassment caused by such an impression being given since their cooperation in the project was invaluable.

The data used came from Southmead's own computer system. We were aware that they included data on children. The simulation model can be used to produce projections for various age groups, but in this case we thought that the numbers were too small to produce reliable results. For simplicity we included the whole of the programme in the projections. Thus children were included in the numbers of patients and in survival curves used to produce projections.

It is important to appreciate that simulation models cannot predict the future. Good models predict what will happen given certain circumstances and can be adapted easily to accommodate changes in policy and practice. In view of the inevitable delay to publication of the paper we could have described the quite recent changes in service provision and costs. Despite this our projections showed that, even without an increased uptake rate, the demand for hospital dialysis facilities would almost immediately be at the former upper limit.

We believe that use of this model by purchasers has improved understanding of the service and its increasing resource demands.

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EDITOR,—P G Bolger and R Davies state that the number of new patients taken on for treatment in Southmead in 1989 was 40 per million population per year. This is exceptionally low: it is lower than the national average, much lower than the modest targets set by the Renal Association of Great Britain, and less than half the rates in other parts of the country, including Cornwall and Wales.

Why is there such a large difference? It cannot be explained demographically. In Wales a deliberate policy decision was made to devolve dialysis facilities to the districts, and the subsequent diaspora of nephrologists away from the teaching centres, together with provision for more hospital based haemodialysis, has led to the rate of new patients being taken on for dialysis being over 100 per million population per year in many areas. A similar pattern has developed in Cornwall, as well as in other parts of Europe where facilities for hospital based haemodialysis are not restricted.

One way to keep the cost of dialysis down is to limit access to it. This is best done by concentrating services in one centre, preferably on the periphery of the catchment area it is supposed to serve. The indifference of many British nephrologists to this situation has become known internationally.² Nephrologists in Britain are apparently content that at least half the people who would benefit from their skills are either not referred or told that they "have the type of kidney disease that does not respond to dialysis treatment."

We believe that the answer is to develop renal services in each district general hospital, but this would undoubtedly increase the total expenditure on renal services, and no district health authority will seek this option unless forced to do so. The treatment is costly but no more so than keeping an elderly demented patient in residential nursing care, and our society prides itself on being able to look after these unfortunate people.

We question who is going to ensure that equitable provision of dialysis is maintained in each district health authority and what powers there will be to correct the situation when it is clearly shown to be deficient.

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Heterosexual AIDS epidemic

EDITOR,—Chris Ford objects that information about AIDS "is still male dominated" and gives examples of recent medical literature that she or he considers ignores women.¹ It is indeed important