clinic, and an abnormally placed testis should be detected.¹ As some undescended testes descend spontaneously we suggest that all boys with an undescended testis at 8 months should be reviewed at 1 year and, if the testis has still not descended, referred to a surgeon so that orchidopexy can be arranged during the second year of life.

To reduce the toll of testicular cancer better health education is required as this would also benefit all potential victims, 90% of whom have normally descended testes. Self examination should be taught at an early age and may lead to earlier presentation of testicular tumours.

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Causes of lower gastrointestinal haemorrhage

EDITOR,—In the article on lower gastrointestinal haemorrhage in the ABC of colorectal diseases diverticular disease heads the list of causes of such haemorrhage in elderly people.¹ The author goes on to point out that although diverticular disease was once considered to be the most common cause of major lower gastrointestinal haemorrhage, many cases are now attributed to angiodysplasia.

Though I accept that massive bleeding may rarely occur from a colonic diverticulum, it is, I believe, a common misapprehension that diverticular disease also causes less severe intermittent blood loss from the lower bowel. In over 30 years' experience of general surgery I cannot remember a single case in which some other cause, usually a polyp or carcinoma, was not found for such bleeding. I believe that it is dangerous to attribute bleeding from the lower bowel to diverticular disease and that full investigation, usually including flexible sigmoidoscopy or colonoscopy, is mandatory.

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Pregnancy associated plasma protein A in Down's syndrome

EDITOR,—Among the maternal blood markers of fetal Down's syndrome reported so far three seem to be much more sensitive than the others. These are human chorionic gonadotrophin (both the intact molecule and its free β subunit), neutrophil alkaline phosphatase, and pregnancy associated plasma protein A (PAPP-A). Nicholas Wald and colleagues' report showing PAPP-A concentrations at 9-12 weeks' gestation to be substantially reduced in 19 pregnancies in which the fetus had Down's syndrome serves to confirm PAPP-A as a potentially important marker.¹ In the previous published series of 14 such pregnancies, however, measurements were made at 6-9 weeks' gestation,^{2,3} so that all the published data relate to a period much earlier in pregnancy than when screening for Down's syndrome is currently performed (15-20 weeks).

We therefore examined PAPP-A concentration at the later gestation in Yorkshire region's screening programme for Down's syndrome. In this, maternal blood is collected for measurement of

α fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin concentration, and residual serum samples are stored at -25°C or cooler. The region is served by a single cytogenetics laboratory, whose records were used to identify 18 cases of Down's syndrome in the screened population. For each case five control pregnancies were found, matched for gestational age. All samples were retrieved from storage and assayed for PAPP-A in two analytical batches, without the person performing the assay knowing which samples were from cases. A radioimmunoassay was used at the Royal London Hospital based on a commercial antibody (Dako) and purified PAPP-A from the University of Odense. All results were expressed in multiples of the normal median (MoM) for the appropriate gestation derived from the regression of PAPP-A concentration on gestation in the 90 controls.

The distribution of concentrations in the cases was lower on average than that in the controls but not substantially so, and the difference was not significant. The 25th, 50th, and 75th centiles were 0.54, 0.87, and 1.11 MoM respectively in the cases compared with 0.69, 0.99, and 1.42 MoM respectively in the controls. The 95% confidence interval for the median in the cases (0.64 to 1.20 MoM) did not overlap with that in either the 6-9 week or the 9-12 week series (0.09 to 0.51 and 0.17 to 0.46 MoM respectively). The same reagents were used in all three series, and our results therefore suggest that PAPP-A concentration is a more sensitive marker in early pregnancy.

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- 1 Wald N, Stone R, Cuckle HS, Grudzinskas G, Barkai G, Brambati B, *et al.* First trimester concentrations of pregnancy associated plasma protein A and placental protein 14 in Down's syndrome. *BMJ* 1992;305:28. (4 July.)
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EDITOR,—Nicholas Wald and colleagues report low maternal serum concentrations of pregnancy associated plasma protein A (PAPP-A) in the first trimester in pregnancies in which the fetus had Down's syndrome.¹ They found no significant relation between the concentration and gestational age in normal women, presumably because of the limited time window (9-12 weeks), and therefore expressed their data as multiples of the median for the whole control group. Other authors have reported increasing PAPP-A concentrations over the first trimester.^{2,3} In our study (of 444 women with fetuses of normal karyotype; serum samples taken at 6-12 weeks) we used the same radioimmunoassay as that used by Wald and colleagues; we found that the PAPP-A concentration increased strikingly over this time.⁴ The relation between

the median PAPP-A concentration and gestation (expressed as days from the last menstrual period) was:

$$\log_e(\text{PAPP-A}) = 0.512 + 0.091d \quad (R^2 = 92\%, \quad p < 0.0001)$$

Should measurement of PAPP-A concentration emerge as a screening test in the first trimester accurate gestational dating will be needed to interpret the result of the test.

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AUTHOR'S REPLY,—It is recognised that pregnancy associated plasma protein A (PAPP-A) concentrations increase with gestational age during pregnancy. As M C M Macintosh and T Chard say, the relevant issue in our study is that, between nine and 12 weeks' gestation, we found no observable association between PAPP-A concentration and gestation so there was no need to generate normal median PAPP-A concentrations specific to gestation. We agree that this should not be taken to mean that gestation could be ignored if measurement of PAPP-A was to be used as a screening test.

More important is to define the gestational period over which measurement of PAPP-A concentration may be a useful screening test. Measurement of PAPP-A concentrations with an enzyme linked immunosorbent assay and using a commercial antibody to PAPP-A (DAKO) at 15-17 weeks of pregnancy in 16 pregnancies in which the fetus had Down's syndrome and 147 in which it did not (controls) indicated that the measurement is not useful at this time; the median value in the pregnancies in which the fetus had Down's syndrome was 1.02 multiples of the median (95% confidence interval 0.81 to 1.28) — that is, virtually the same as that in the control pregnancies of the same gestational age (NW, AV, unpublished data).

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Notifying contacts of people with HIV infection

EDITOR,—R A Keenlyside and colleagues report a useful survey of attitudes to tracing and notifying contacts of people with HIV infection¹; their introduction and discussion, however, show that they are unaware of the General Medical Council's clear guidelines on notification of partners introduced in 1988.²

According to the guidelines, doctors can disclose the HIV status of patients to their sexual partners without the patients' consent. Before doing so,