Letters to Editor

False positive results with Pregnosticon pregnancy test

The experience of Dr Hunter and Mr Gray with Pregnosticon,¹ a haemagglutination inhibition test for pregnancy, is of interest. It is not clear from their account whether the eight positive Pregnosticon reactions occurred on the same day and with the same batch of reagents. In our laboratory specimens are occasionally received which cause a partial inhibition of haemagglutination. Such reactions are not recorded as positive and the tests are repeated the next day, when the result has always been correctly negative.

Immunological pregnancy tests can be affected adversely by non-specific factors, including detergents. About 5000 of the 20 000 specimens received annually come in bottles, usually without, but not always, some of their former contents. Hair shampoo bottles are popular, and urines from these may interfere with the normal test reaction.

We have used Pregnosticon since 1963 and tested more than 405 000 urines with this reagent. The overall accuracy of the test, based on the clinical diagnosis for 52 606 women, is 98.7% with an accuracy of 98.1–100% between 21 batches. Analysis of the results shows that a positive result in the absence of clinical evidence of pregnancy might be expected once in 2600 tests. As information accumulates about the incidence of menstrual and very early abortions the probability that these false positives are correct must also be considered.

In a recent comparative study between a slide test (Pregnosticon Neoplano Duoclon, sensitivity 500 IU human chorionic gonadotrophin/l) and a haemagglutination inhibition test (Pregnosticon "ALL-in," sensitivity 1000 IU human chorionic gonadotrophin/l) there was complete agreement between the two tests in 993 of 1015 urines. The difference was due to 22 urines giving a positive Neoplano, negative Pregnosticon reaction. Clinical diagnosis subsequently confirmed that the 22 urines were from women with early pregnancies. The less sensitive haemagglutination inhibition test was never positive when the more sensitive direct latex agglutination test was negative.

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Reference

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Susceptibility of *Campylobacter* spp to inks

I read with interest the article by Mr Bolton and his colleagues,¹ in which they described the susceptibility of *Campylobacter* spp to various dyes and chemicals for use in a biotyping scheme.

I should like to report an observation I made during a similar investigation. Eight strains consisting of *Campylobacter jejuni*, *Campylobacter coli*, and *Campylobacter lariidis* were streaked across blood agar (Lab M—WBA) test plates. Bacteruritest dipstrips (Mast) which had been soaked in undiluted writing ink (Super Quink; Parker Pen Co Ltd) and dried were placed on the agar surface at right angles to the bacterial streaks. All plates were incubated microaerobically at 37°C for 48 h. Growth of the eight strains was not affected by the green, red, or royal blue inks, but all were inhibited by the black ink. After discussions with the manufacturer, the most likely difference between these inks is either the formulation of the biocide or the pH. Other workers may consider that this observation is worthy of further investigation with a larger number of strains.

This work was carried out at the Luton Public Health Laboratory.

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Reference

- ¹ Bolton FJ, Holt AV, Hutchinson DN. *Campylobacter* biotyping scheme of epidemiological value. *J Clin Pathol* 1984;37:677–81.

Small intestinal mucosal fat in childhood enteropathies

We read with interest the article by Variend *et al*¹ entitled "small intestinal mucosal fat in childhood enteropathies." The authors state that "mucosal fat in small intestinal disease has not been previously investigated."

We presented a paper at the IXth European Congress of Pathology held at Hamburg in September 1983 on "Lipids in enterocytes".² We found lipid vesicles in the enterocytes of three adult patients suffering from diarrhoea with steatorrhoea. Electron microscopical studies showed that the lipid vesicles were partly membrane bound and were in close relation with the smooth endoplasmic reticulum, less often in the Golgi region. The aetiology of this condition remains obscure.

Puzzled by these findings, we reviewed the endoscopic and tube biopsies of the duodenum and jejunum examined at our department during 1982. Of a total of 650 biopsies, we screened those with villous atrophy in coeliac disease (new and treated cases) and found lipids in the enterocytes of 10 adults and three children.

From the studies of Riley and Glickman³ we suggest that the accumulation of lipids in the smooth endoplasmic reticulum is probably due to a disturbance of triglyceride resynthesis and phospholipid reacylation; their presence in the Golgi apparatus would indicate a disturbance in their glycosylation.

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- ² Widgren S, Bergoz R, Voirel M. Lipids in enterocytes. *Path Res Pract* 1983;178:173.
- ³ Riley JW, Glickman RM. Fat malabsorption. Advances in our understanding. *Am J Med* 1979;67:980.

On the naming of dyes

Today's histologists are becoming more colour conscious. Modern colour film entices them to experiment with dyes invented since the days of van Gieson, Mallory, Heidenhain, and Masson.

In the time of those leaders there was no directory or index of dyes other than Schultz's *Farbstofftabellen*. This has been largely superseded by the Anglo-American *Colour Index*, now in its 3rd edition.¹ The latter, with its mass of international information, skilfully classified and arranged, is kept up to date with supplements. It is, however, very costly. Fortunately, much of

the information in the *Colour Index* of possible interest to histologists is available in the 9th edition of *Conn's Biological Stains* by Lillie.²

Lillie provides for each dye used or likely to be used by biological scientists, the common synonyms including brand names, the formula, and its five figure number in the *Colour Index*, part II. Also with this he gives the group category of the dye, based on the practical application to textiles—for example, acid dyes, direct dyes, basic dyes, mordant dyes, and so on. Thus on page 121, for example, Acid Red 44, variously known as Ponceau 6R, Scarlet 6R, Bordeaux G with brand name suffixes, has its formula and its number 16250, along with molecular weight and comments on its use and users. The group coding Acid Red 44 is just as specific as the CI number; in addition, it signifies a red anionic dye and is more memorable. Similarly, Pararosanilin, Magenta O, the chief constituent of the mixture called basic fuchsin is Basic Red 9, and Celestin Blue, Coreine 2R, Gallo Sky Blue is Mordant Blue 14.

Writers of technical texts^{3,4} and laboratory suppliers are gradually taking notice of this nomenclature. I would plead with editors that they insist on the use of group number, and with authors that they ask the suppliers to use the group number and to state the manufacturer of the dye they supply.

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References

- ¹ *Colour index*. 3rd ed. Bradford: The Society of Dyers and Colourists, 1971.
- ² Lillie RD. *Conn's biological stains*. 9th ed. Baltimore, Maryland: Williams and Wilkins, 1977.
- ³ Bancroft JD, Stevens A. *Theory and practice of histological techniques*. 2nd ed. Edinburgh: Churchill Livingstone, 1982.
- ⁴ Drury RAB, Wallington EA. *Carleton's histological technique*. 5th ed. Oxford: Oxford University Press, 1980.

Factor VIII concentrate as a source of fibronectin for replacement therapy

Dr JT Reilly and others¹ have advocated the use of factor VIII concentrates as a source of fibronectin for clinical use, chiefly because they are said to contain more fibronectin per gram total protein than cryoprecipitate.

Fibronectin antigen and specific fibronectin content of 20 batches of NHS factor VIII concentrate

	Mean value (SD)	Range
Fibronectin antigen	5.2 mg/ml (1.5)	2.4–8.8 mg/ml
Total protein	43 mg/ml (8)	25–57 mg/ml
Mean % fibronectin	12.5% (3.1)	7–21%

Fibronectin antigen was assayed by the Laurell method of rocket immunoelectrophoresis using chromatographically purified plasma fibronectin, extinction coefficient $E_{280}^{1\text{ mg/ml}} = 1.28$. With this system, normal plasma controls contained about 300 $\mu\text{g/ml}$ fibronectin antigen.

The proportion of fibronectin to total protein in the NHS concentrate is substantially lower than that stated by Reilly *et al.* In addition, we believe that it is unlikely to be 50–60% higher than that in commercial factor VIII concentrates, as suggested.

Fibronectin antigen was measured in a series of batches of factor VIII concentrate made in Blood Products Laboratory during 1982; total protein (biuret) was measured in every batch as part of routine quality control. Twenty such batches, redissolved according to instructions on the label, were assayed (Table).

In the course of preparing factor VIII concentrate from cryoprecipitate on a large scale, fractionators deliberately remove much of the fibronectin from the factor VIII. On average, the total fibronectin content of 1 litre of fresh frozen plasma would be 300 mg. The cryoprecipitate from 1 litre of plasma contains around 200 mg fibronectin. The same amount of cryoprecipitate yields only 78 mg fibronectin when processed further to give 15 ml (one vial) of factor VIII concentrate. Although factor VIII concentrate contains fibronectin at a higher specific activity than in cryoprecipitate, it is a wasteful source of fibronectin.

Infusion of any of these concentrates into patients would carry a risk of transmitting virus infections, particularly non-A, non-B hepatitis, which would have to be weighed against any benefit predicted. In our opinion, the published case for intravenous supplementation of fibronectin is circumstantial and the use of a crude source of supplementary fibronectin in the complex circumstances prevailing—for example, in extensive burns, abdominal sepsis—would be inconclusive. With the advent of virus inactivation methods, the element of risk might be reduced sufficiently to justify a clinical trial of fibronectin concentrates. Concentrates of purified fibronectin derived from this source are available from Blood Products Laboratory for laboratory study. Mean-

while, we hope that scarce resources of NHS factor VIII concentrate will not be diverted as a trivial and potentially hazardous source of fibronectin in uncontrolled trials which are unlikely to prove or disprove its efficacy.

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Reference

- ¹ Reilly JT, McVerry BA, Mackie MJ. Fibronectin in blood products—an in vitro and in vivo study. *J Clin Pathol* 1983;**36**:1377–81.

Dr Reilly and others comment as follows:

We would like to comment on the several points raised by Dr Smith and his colleagues. Firstly, our mean value for the proportion of fibronectin to total protein in the NHS concentrate (16%) is not, as suggested, substantially higher than their value (12.5%) and lies well within their quoted range. Secondly, at no point in our paper did we advocate the routine use of factor VIII concentrate for fibronectin replacement therapy in patients with sepsis, shock etc. Although we quoted data suggesting that replacement therapy may be beneficial in certain cases, we appreciate that these studies, carried out on relatively few patients, require confirmation. Furthermore, we clearly emphasised in our paper the well known potential hazards of infusing such concentrates into patients.

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