has been found a satisfactory way of preserving the quality of the preparations, giving superior results to simple air drying which causes distortion and shrinkage of cells with considerable loss of surface detail. Critical point drying which has also been shown to be superior to simple air drying in this respect (Polliack *et al*, 1973) can be used with the present method, but special facilities are required.

Preliminary observations using the method indicate its potential value in studying cellular function in the inflammatory reaction in patients with malignant blood disorders and other disease states.

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Letters to the Editor

Rheovirus and E. coli in infantile enteritis

The recent article by Bishop *et al* (1976) reports inconclusive results which may be interpreted in different ways. These authors studied an outbreak of acute enteritis in the neonatal wards of a Melbourne hospital; 32 babies were at risk and 15 developed diarrhoea. *Escherichia coli* O111. H21 was found in 11 babies with diarrhoea and in five of those without diarrhoea, while a reovirus-like agent was found in eight babies with diarrhoea and in three without diarrhoea. On the basis of these results the authors conclude 'that the epidemic was primarily caused by infection with the reovirus-like agent' and they 'do not consider that the strain of *E. coli* O111 isolated in this study was primarily implicated in the aetiology of the epidemic'. *E. coli* O111 was isolated three days before the onset of diarrhoea in two babies, coincident with onset in four babies, and seven days after onset in one baby. In four cases the relation of acquisition to onset of symptoms was not determined. On the basis of these observations it was concluded that 'Isolation from rectal swabs (of *E. coli* O111) did not correlate with the presence and absence of symptomatic illness'. No attempt was made to relate the acquisition of reovirus-like particles to the onset of symptoms. The authors seem willing to apply the principles of epidemiology only in support of the pathogenicity of reovirus. However, the same principles should be applied to enteropathogenic *E. coli*, and the evidence from this outbreak could suggest equally well that *E. coli* O111 was an epidemic agent.

Dr Bishop and her colleagues failed to demonstrate enterotoxin production by the strains of *E. coli* O111.H21 and use this finding in support of their conclusion. However, enterotoxin production should not be considered as the sole criterion of enteropathogenicity. We have studied epidemic strains of *E. coli* from well-documented, notorious outbreaks of infantile enteritis in the United Kingdom and none of these strains could be shown to produce enterotoxin using the infant mouse and the Y1 and CHO tissue culture systems (Gross *et al*, 1976). Nevertheless there is good epidemiological evidence to support the aetiological role of these epidemic strains in the outbreaks. We consider that this epidemiological evidence establishes the enteropathogenicity of the strains which we studied, and the failure to demonstrate enterotoxigenicity does not invalidate this conclusion. These strains may produce enterotoxin at a level below that detectable by the current test systems or may produce an enterotoxin which differs qualitatively from the enterotoxin detected by these tests. Alternatively, enterotoxin may not play a part in the pathogenesis of infantile enteritis caused by enteropathogenic *E. coli*.

It is an admirable aim to search for new causes of disease but it is a dangerous policy to minimize the importance of established pathogens. Bacteriologists must remain alert to the danger of outbreaks of infantile enteritis due to *E. coli*; those involved in the Teesside (*Lancet*, 1968; *British Medical Journal*, 1968), Manchester (Jacobs, 1969; Jacobs *et al*, 1970), and Glasgow (Rowe and Gross, 1971; Love *et al*, 1972; Kennedy *et al*, 1973) outbreaks are well aware of the virulence of some strains of *E. coli*.

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The authors have replied as follows:

As stated in our article, we believe that the epidemic we studied was primarily caused by infection with the reovirus-like agent rather than by the strain of *E. coli* O111 isolated. Our belief is based partly on epidemiological evidence, and partly on the failure to demonstrate enterotoxin production by this strain of *E. coli* O111. We do not share the belief that this latter fact can be overlooked.

To enlarge on the epidemiological findings: the reovirus-like particle was seen in eight babies with diarrhoea from whom faeces were obtained on the day before onset of symptoms (1), day one (3), day two (2), day three (1), and day four (1) after onset of symptoms. No virus particles were seen in seven babies with diarrhoea examined five days before onset of symptoms (2), on day three (2), day five (2), and day nine (1) after onset. We can sum this up by saying that reovirus-like particles were located in eight of 10 babies with diarrhoea in whom faecal specimens were examined at the optimal time in relation to onset of symptoms (from one day before onset to four days after onset). The strain of *E. coli* O111 was repeatedly isolated from four babies remaining in the ward 30 days after the outbreak began. It did not cause a renewed outbreak of diarrhoea in newly admitted babies when the ward was reopened.

We do not wish to minimize the importance of a virulent strain of *E. coli* in a hospital nursery, or to cast doubt on the aetiological agents of the epidemics on Teesside, in Manchester, and in Glasgow. The clinical symptoms recorded in babies in those outbreaks differ from those observed in the Melbourne outbreak. We urge that microbiologists remain alert to progress in virological and bacteriological techniques, and that further epidemics of neonatal diarrhoea should be studied using new methods as well as old.

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More information please about commercial reagents

Commercial companies who manufacture complex laboratory equipment for use in Health Service laboratories and which is dependent upon patented materials including reagents would seem to have a moral obligation to provide published scientific evidence of the derivation of the data usually provided with them. This can be illustrated by the Coulter Counter Model 'S' System. Coulter Electronics Ltd supply 4C, a preserved preparation against which the instrument is calibrated. In our laboratory we have devised a number of quality control procedures to monitor the instrument's performance. These employ 4C as well as our own specially preserved blood samples. Consequently the validity of our results (especially for mean cell volume, MCV) is dependent to some extent on the reliability of 4C.

I would like to suggest that since this preparation plays such a crucial role in quality control the Company should make more information available about it (while still maintaining their legitimate commercial secrecy). I would also like to suggest that when a qualitative or quantitative change is made in any of the reagents used in the Coulter 'S' (eg, Isoton or Lyse S) the Company should publish data showing that the old and new reagents give identical results with specimens from patients as well as from healthy individuals.

There are two recent occurrences which exemplify our dependence in this way on Coulter Electronics Ltd.

1 The MCV of 4C and the trapped plasma correction. Up to some five months ago the MCV of 4C was identical with the value that would have been derived from the packed cell volume (determined by microhaematocrit) and the visual cell count. This value is an overestimate as the packed cells include trapped plasma. The MCV of 4C (Coulter assay value) has now been altered to allow for trapped plasma and has therefore been reduced by some 3-4 fl. This implies that in laboratories where 4C is the sole preparation used to calibrate the Coulter 'S' all MCV values must have been increased by about 5% for normals and possibly more for patients with, for example, a microcytic anaemia. Clearly, the haematocrit and mean cell haemoglobin concentration will also have been affected. A disturbing result of a once and for all change of this nature is that in practice it may not be possible to update all medical staff to whom the results are sent. Consequently the systematic shift in the patients' indices may be misinterpreted.

Although the Company indicated in a memorandum that this change had taken place, they did not spell out its consequences nor state exactly when it had occurred.

2 Isoton and Isoton II. In May 1976 the present diluent Isoton is to be replaced by an improved version, Isoton II. Coulter Electronics Ltd have stated that the MCV of 4C will change by 3-4 fl and that the assay value will be altered to take this into account. They also state that no recalibration of the Coulter Counters is required for fresh blood specimens but have produced no evidence in justification. We ourselves will therefore have to use both the old and the new Isoton to analyse specimens from healthy individuals and (in particular) patients, and will not have confidence in results obtained using the new Isoton until this has been done.

I appreciate that Coulter Electronics Ltd may not have ready access to the necessary specimens, but I feel sure that some hospital laboratories would be prepared to cooperate with them in a suitable trial.

To summarize, this letter is a plea for more detailed information about commercial products. It can be made especially to Coulter Electronics Ltd because, in our experience, this Company is usually reliable and always helpful.

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