Matters arising

captopurine, and local steroid cream. Bleeding problems worsened and she became dependent on transfusions. Platelets remain around $6 \times 10^9/l$ and white cell count is normal but with highly dysplastic neutrophils at the time of writing.

These two patients showed red cell hypoplasia with refractory anaemia and later developed myelodysplastic and myeloproliferative features. Both had a normal karyotype, ran a chronic course, and developed a second malignancy. Neither fits easily into the current classification of myelodysplastic syndromes.

MK COOK
Bangour Laboratories,
Bangor General Hospital,
Broxburn,
West Lothian,
EH52 6LR

Reference

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Differential diagnosis of metastatic undifferentiated carcinoma

Ellis and Hitchcock recently described the possible use of a panel of antibodies in the differential diagnosis of metastatic undifferentiated carcinoma with an unknown primary site.¹ It was suggested that there are characteristic patterns of immunoreactivity which may help indicate the primary site. This is clearly an important study as it paves the way for histopathologists to provide the clinician with valuable information in the hunt for the unknown primary. This is a not uncommon clinical problem and, with improvements in therapeutic options for some tumours, one of real practical importance.^{2,3} But we would welcome the authors' comments regarding the following points.

Given that little information about the "differentiation" of these cases is provided, they may just be relatively typical examples rather than difficult, poorly differentiated tumours which are so characteristic of the difficult cases where histopathologists depend on help from immunohistological techniques. There is also some evidence to suggest that metastatic deposits are less well differentiated than primaries and exhibit variable, but often pronounced, phenotypic diversity. Therefore the hypothesis that

immunophenotypic patterns may indicate site of origin must be tested on secondary deposits, preferably those that presented as adenocarcinoma of unknown origin. Such a study could be based on cases in which post mortem examination or other investigation defined the primary site of disease.

A further point of relevance to the problem of the unknown primary relates to the identification of endocrine neoplasms. Hainsworth *et al* identified 29 patients who presented with metastatic carcinoma of unknown primary in which electron microscopic examination or immunohistochemical techniques (primarily using anti-NSE) indicated a neuroendocrine tumour.⁴ In four patients a well recognised tumour was eventually found (gut carcinoid $n=2$, oat cell in lung $n=1$, mediastinal germ cell tumour with pronounced neuroendocrine differentiation $n=1$). Although the total population from which these cases were drawn is not stated, they do remark that they were found in a single institution and that 24 were found between 1981 and 1987, suggesting that they may be relatively common. Given these data, it may be that antibodies which recognise endocrine cell differentiation should be included in panels for the characterisation of the "unknown primary".

PA HALL,
ICRF, Lincoln's Inn Fields,
London,
DA LEVISON,
Department of Histopathology,
Guy's Hospital,
London

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Drs Ellis and Hitchcock comment:

To illustrate the potential of tumour marker immunohistology we felt it essential to determine tumour marker profiles of adenocar-

cinomas at their known site of origin prior to a study of metastatic tumour from an unknown primary site. The baseline information we presented justifies detailed study of metastatic tumours. We would clearly support the view that study of the primary and secondary tumour from patients presenting with metastatic disease, in whom the primary is subsequently identified, is vital before this approach could be advocated as a useful routine procedure.

Our work was based purely on adenocarcinomas. The tumours from each primary site were consecutive cases presenting to our department and included a range of tumours with varying differentiation. Again for the above reason, we feel it was important to study a representative range of tumours from a given site rather than to select unusual or poorly differentiated examples.

This type of approach could be applicable to all forms of metastatic tumour. In our study we chose to examine only adenocarcinoma because of the wide range of tumour markers available for these tumours. As Hall and Levison point out, other groups have shown the value of new endocrine markers to identify tumours of neuroendocrine origin.

We suggest that use of immunocytochemistry on metastatic tumours to determine a likely site of origin has considerable potential. We have illustrated that in adenocarcinoma a panel could help to identify the site of origin. In undifferentiated tumours other such panels may prove helpful in identifying the cell type or site of origin.

Role of Verotoxin producing *Escherichia coli* in the aetiology of haemorrhagic colitis

We read with some surprise the recent report by Larson and Welch.¹ Our own study of the incidence of Verotoxin producing *Escherichia coli* (VTEC) in haemorrhagic colitis was conducted from 1 January 1986 to 31 December 1987.² During this time we searched for VTEC in faecal samples from 40 patients with haemorrhagic colitis (sudden onset of grossly bloody diarrhoea, usually with an absence of fever but sometimes preceded by abdominal pain and cramps and watery non-bloody diarrhoea), and 229 age and sex matched control patients with acute non-bloody diarrhoea. Faecal samples were examined for the presence of *E coli* 0157 by culture on sorbitol MacConkey agar (Oxoid CM813), followed by biochemical identification of all apparently sorbitol negative colonies. Those confirmed as sorbitol negative *E coli* were checked for agglutination with *E coli* 0157 antiserum (Difco) using