

Appearance of the sensitivity plate

*Staphylococcus aureus*. The staphylococcus could not be recovered from other areas of the sensitivity plates, which consisted of a pure semiconfluent growth of *Streptococcus faecalis var zymogenes*.

The appearance of the *Staphylococcus aureus* colonies only in discrete rings associated with particular antibiotic sensitivity discs is explained by an antagonism of the staphylococcus by the streptococcus. When a mixture of the two organisms is used as an inoculum for DST sensitivity plates, the staphylococcus forms colonies only where the streptococcus is preferentially inhibited by an antibiotic.

When antibiotic sensitivity determinations of the two organisms were carried out on DST agar alone, only with mezlocillin, trimethoprim, and nitrofurantoin did the staphylococcus yield a smaller zone than the streptococcus. On DST sensitivity test plates prepared from mixed inocula of the two organisms, staphylococci appeared as rings of growth around these antibiotics.

On ordinary blood agar staphylococci appeared similarly as rings of growth around mezlocillin and nitrofurantoin, but strangely appeared as a disc of growth growing around and right up to the trimethoprim disc. On their own, on blood agar both cultures grew almost right up to the trimethoprim disc. Haemolysis of the medium by the streptococcus was inhibited around the trimethoprim disc, however, and a ring of maximum haemolysis appeared as a ring around but some distance from the disc. This inhibition of haemolysis, but not growth, appeared to coincide with an inhibition of anti-staphylococcal activity by the streptococcus in the presence of certain concentrations of trimethoprim.

The inhibitory activity shown by the streptococci showed the properties previ-

ously ascribed to some streptococci. By the methods of Kekessy and Piguët<sup>3</sup> the inhibitory range was shown to be restricted to related *Streptococcal* spp and to *Staphylococcus* spp, and a  $\beta$ -haemolytic activity associated with bacteriocin activity has been previously recorded with *S faecalis var zymogenes*.<sup>4</sup> The properties of the bacteriocin like activity produced by *S faecalis var zymogenes* and reported here most clearly resembled those described by Brock<sup>5</sup> as a type I bacteriocin.

These observations are reported for interest because they show one disadvantage that may ensue from using the primary urine culture method adopted here. If the inhibitory culture had been uniformly more antibiotic resistant than the other culture, the presence of the inhibited culture would have been overlooked and this might not have been corrected by reference to the primary isolation plates.

The effect which subinhibitory concentrations of trimethoprim may have on the production of metabolites by *S faecalis var zymogenes* and the inhibitory effect which that organism may exert on other Gram positive cocci is worthy of note because of the recent upsurge in interest in the effects of antibiotics at suboptimal concentrations.

JG BARR

ETM SMYTH

Department of Clinical Bacteriology,  
Royal Victoria Hospital,  
Grosvenor Road,  
Belfast,  
Northern Ireland

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#### Measuring melanomas: the Vernier method

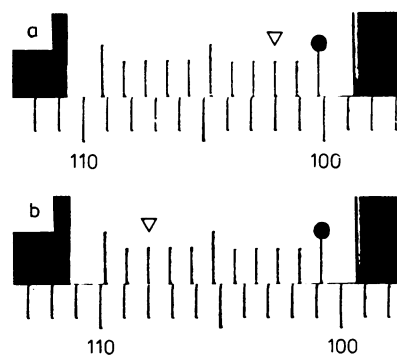
Breslow<sup>1,2</sup> has clearly demonstrated that tumour thickness is the single most important histological criterion in determining the prognosis of stage 1 malignant

melanoma and in particular is a better measure than the level of invasion of the tumour. He measured the thickness from the granular layer of the epidermis to the deepest part of the tumour using an ocular micrometer and found a 100% 5 year tumour free survival rate for melanomas less than 0.76 mm thick, whilst those greater than 1.50 mm in thickness carried a bad prognosis.

This observation has now been confirmed by other workers,<sup>3-5</sup> but thickness does not seem to be uniformly included in histopathological reports of melanomas. We think that this may be because pathologists think that they need an ocular micrometer or a computerised image analysis system<sup>6</sup> to make the measurement and may not have the equipment readily to hand.

However, almost all modern laboratory microscopes have Vernier scales fitted on their stages, which are principally designed to give grid references for slides. In a brief survey of colleagues we found that many did not understand the principle or application of these scales, which actually provide an excellent way of measuring the thickness of melanomas.

The section of the melanoma should be orientated on the mechanical stage so that the tumour is perpendicular to one of the axes. The tumour is then aligned with a fixed point such as the edge of field of view. If a teaching pointer is fitted to the microscope this can be used instead. First of all the granular layer is aligned to the fixed point. The position on the Vernier scale is



Photographs of a Vernier scale on a microscope stage in two different positions, (a) showing a reading of 100.2 mm (arrowhead), and (b) showing a reading of 100.8 mm (arrowhead). The difference between the two readings is therefore 0.6 mm.

noted to the nearest tenth of a millimetre. Then the slide is moved to align the deepest part of the tumour to the same fixed point and a second reading taken. The tumour thickness can then be derived by subtracting one reading from the other (Figure).

This is a simple and reliable method. The measurement can be made using any combination of objective and eyepiece magnification and tube length. No conversion factors or calculations have to be used, thus eliminating further sources of error.<sup>6</sup> The measurement is only made to the nearest tenth of a millimetre but in most cases the lesion can be easily assigned to one of the three prognostic categories (<0.76 mm, 0.76–1.50 mm and >1.50 mm) without measuring to the nearest hundredth of a millimetre. The only problem we find amongst our colleagues is uncertainty regarding the working of Vernier scales. These were invented by the Burgundian Pierre Vernier (c. 1580–1637) and described in 1631 in his book *La Construction, l'usage, et les propriétés du quadrant nouveau de mathématique*.<sup>7</sup> Briefly, there is a short scale 9 mm long, divided into 10 equal 0.9 mm long parts, sliding on a scale graduated in millimetres. When one examines the short scale one of its 10 graduations will be exactly in line with a mark on the long scale. This then gives the decimal place value between 0.1 and 0.9 mm.

If one is unsure of the technique, or of the accuracy of the scales on a particular microscope, then a slide bearing a known standard scale can be employed, as one would in calibrating an ocular micrometer. We hope that histopathologists will now be encouraged to use this simple technique to report the thickness of melanomas in all cases.

N KIRKHAM  
DWK COTTON

Pathology Department, LE56,  
Southampton General Hospital,  
Southampton SO9 4XY

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## Routine bone marrow aspirations during maintenance treatment in acute lymphoblastic leukaemia do not improve survival

In the paper by Franklin<sup>1</sup> the value of routine bone marrow aspirations in terms of their contribution to prognosis has been questioned.

In 109 children with acute lymphoblastic leukaemia diagnosed in our department between January 1976 and June 1982 and treated with AIL-AIEOP (Italian Paediatric Cooperative Group for Therapy of Acute Leukaemia) 7601, 7602, 7901, 7902, and 7903,<sup>2</sup> 1308 routine bone marrow aspirations and 108 non-routine bone marrow aspirations were performed during maintenance treatment and after stopping treatment. Routine bone marrow aspirations were carried out at two to three monthly intervals; non-routine bone marrow aspirations were performed when haematological relapse was suggested by any of the following: peripheral blood count anomalies (circulating blast cells, haemoglobin concentration less than 10.5 g/dl, lymphocytosis more than 70%, platelet count less than  $120 \times 10^9/l$ ), hepatomegaly (liver  $\geq 3$  cm) or splenomegaly (spleen  $\geq 1$  cm), or both, not attributable to infection, malaise, bone pains, or extramedullary relapse.

Nine out of 1308 routine bone marrow aspirations (0.7%) indicated relapse and 21 out of 108 non-routine bone marrow aspirations (19.5%) confirmed the suspicion of haematological relapse ( $p < 0.001$ ). Apart from the presence of circulating blast cells, the predictive parameters for haematological relapse were: thrombocytopenia ( $p < 0.003$ ), bone pains ( $p < 0.004$ ), hepatomegaly ( $p < 0.04$ ), and splenomegaly ( $p < 0.02$ ). Of 30 relapsed patients, 27 died and three are surviving

(follow up to 31 December 1982) after 15, 12, and 24 months. (In the last two cases bone marrow transplantation was performed after the second remission.) The mean survival duration after haematological relapse was  $8.7 \pm 5.5$  months in the routine bone marrow aspiration group and  $9.5 \pm 8.1$  in the non-routine bone marrow aspiration group (NS).

Our study which was carried out on a considerable number of bone marrow aspirations confirms that routine bone marrow aspiration is not an effective diagnostic procedure for detecting haematological relapse. The duration of survival was the same both for patients whose relapse was detected by routine bone marrow aspiration and for those in whom relapse was suspected clinically.

In conclusion, as there is no evidence of any advantage from routine bone marrow aspirations, which are a stressful procedure for children, their periodical performance should be discontinued.

ROBERTO MINIERO

GUIDO PASTORE

PAOLA SARACCO

Department of Paediatrics,

University of Turin

Pizza Polonia 94,

10126 Torino,

Italy

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## Book reviews

**Immunological Investigation of Lymphoid Neoplasms.** Practical Methods in Clinical Immunology Series. Vol 6. GT Stevenson, JL Smith and TJ Hamblin. (Pp 91; £18.) Churchill Livingstone. 1983.

There is a tendency amongst oncologists to categorise cases of non-Hodgkin's lymphoma according to their prognosis and to



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N Kirkham and D W Cotton

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