usually deposited in periarticular sites.\(^1\) Although AH was a consideration in this case because of the history of dialysis,\(^2\) the ultrastructural features of β2 microglobulin are thick curvilinear fragments of 8–10 nm diameter.

Overall, acute bowel infarction and perforation in amyloidosis are rare, and are usually seen only in cases of systemic disease. More commonly, AL results in chronic intermittent bowel obstruction as a result of gut wall deposition of amyloid.\(^3\) The rare cases of gut perforation related to AA have implicated preferential amyloid vascular deposition. In this unique case, the clinical symptoms of acute bowel obstruction complicated by perforation can be explained by an unusual pattern of amyloid deposition in AL, involving both blood vessels and muscularis. Recognition of this rare possibility may facilitate earlier diagnosis in this disease.

### References


## Table 1: Allergy testing results

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Skin prick testing</th>
<th>Specific IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wheal (mm)</td>
<td>Flare</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>--------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Grass pollen mix</td>
<td>3</td>
<td>++</td>
</tr>
<tr>
<td>Cat dander</td>
<td>4</td>
<td>++</td>
</tr>
<tr>
<td>Dermatophagoides pteronyssinus</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Dermatophagoides farinae</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Fresh Quorn mixed with saline</td>
<td>7</td>
<td>++</td>
</tr>
<tr>
<td>Alternaria alternata</td>
<td>2</td>
<td>4.1</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Cladosporium herbarum</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Aureobasidium pullulans</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

In the skin prick test histamine produced a 6 mm wheal and ++ flare, and saline produced a 0 mm wheal and no flare. Results were those seen 15 minutes after using AUK standardised lancets and skin prick test reagents. The specific IgE tests were performed by Sheffield Protein Reference Unit. When Quorn was used as the allergen a small piece of fresh quorn burger was mixed with saline, and a single drop of liquid from the mixture was put on the patient’s forearm as with the other skin prick reagents. No specific IgE was detected to two other fusarium species, F culmorum and F oxysporum. Alternaria alternata, Aspergillus fumigatus, and Cladosporium herbarum are reported to crossreact with Quorn. There was a heavy growth of Aureobasidium pullulans in the patient’s home (no tests available to other species isolated). ND, not done.
200–3000 fold.7 The diversity of fungal allergens is a challenge for successful immunotherapy.

A reduction in occupational exposure to fungi may be achieved using helmets with filtered air (which may remove up to 98% of spores), improving ventilation, and controlling humidity. Fungi in dwellings generally have no specialised spore liberation mechanisms and largely depend on disturbance. Spore wall structure determines whether allergens are already available on the surface, and whether the spores can remain airborne.

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References

Tumour cells produce receptor activator of NF-κB ligand (RANKL) in skeletal metastases

Osteolytic bone destruction is a common complication of tumours that metastasise to bone. Several solid tumours, most notably breast carcinoma, lung carcinoma, and prostate carcinoma, commonly metastasise to bone in patients with advanced disease, where they cause osteolysis and associated pain, hypercalcaemia, and fracture. It is generally accepted that osteoclasts are the only cells capable of resorbing mineralised bone. In osteolytic metastases, it has been shown that tumour cells direct osteoclastic bone resorption through a vicious cycle:1 in particular, tumour cell produced parathyroid hormone related protein (PTHrP) facilitates bone resorption and, as a consequence, transforms growing factor β2 is released from the bone matrix and promotes the progression of bone metastases by further inducing PTHrP production by tumour cells. Other tumour cell products, such as macrophage colony stimulating factor, interleukin 6 (IL-6), IL-11, and tumour necrosis factor α, have also been shown to be associated with tumour induced osteolysis.

However, with the identification and characterisation of a direct stimulator of osteoclastogenesis—the receptor activator of NF-κB ligand (RANKL, also known as ODF, OPGL, and TRANCE)—a final common pathway for osteoclastic bone destruction has emerged. A variety of osteoerotic factors, such as 1,25-dihydroxyvitamin D3, prostaglandin E2, parathyroid hormone, IL-6, and IL-11, have been shown to mediate osteoclast differentiation through the upregulation of RANKL expression or the downregulation of osteoprotegerin (OPG; the decoy receptor of RANKL) expression in osteoblast/stromal cells.9 There is also experimental evidence that tumour produced PTHrP may stimulate osteoclastic bone resorption by enhancing RANKL expression and reducing OPG expression in the osteoblast.7 However, whether tumour cells directly produce RANKL, which subsequently mediates osteolysis in metastatic skeletal lesions, has not been determined.

To this end, we have investigated the expression of RANKL in the skeletal lesions of patients with carcinomas that had metastasised to bone. Sixteen cases, including breast carcinoma (four cases), lung carcinoma (six cases), prostate carcinoma (two cases), and follicular thyroid carcinoma (four cases), were collected during surgery of pathological fractures. Histological confirmation of the diagnosis in each case was based on the review of routinely prepared paraffin wax embedded tissue sections. Immunohistochemical staining of skeletal lesions in bone metastases in comparison with the primary tumours of the same patients. Brown and colleagues7 reported that RANKL was heterogeneously expressed in 10 of 11 prostate carcinoma specimens, and the proportion of tumour cells expressing RANKL was significantly increased in all bone metastases in comparison with non-osseous metastases or the primary prostate tumour. Whether RANKL expression in the primary tumour is predictive of a possible propensity towards skeletal metastasis remains to be seen and could be the focus of future studies.

Acknowledgements
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Table 1 A list of tumour bone metastases and RANKL immunoreactivity

<table>
<thead>
<tr>
<th>Case</th>
<th>Primary site</th>
<th>Diagnosis</th>
<th>RANKL immunoreactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast</td>
<td>adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>2</td>
<td>Breast</td>
<td>adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>3</td>
<td>Breast</td>
<td>adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>4</td>
<td>Breast</td>
<td>adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>5</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>6</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>7</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>8</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>9</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>10</td>
<td>Lung</td>
<td>adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>11</td>
<td>Prostate</td>
<td>adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>12</td>
<td>Prostate</td>
<td>adenocarcinoma</td>
<td>85% Faint</td>
</tr>
<tr>
<td>13</td>
<td>Thyroid</td>
<td>follicular adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>14</td>
<td>Thyroid</td>
<td>follicular adenocarcinoma</td>
<td>95% Faint to intense</td>
</tr>
<tr>
<td>15</td>
<td>Thyroid</td>
<td>follicular adenocarcinoma</td>
<td>85% Faint</td>
</tr>
<tr>
<td>16</td>
<td>Thyroid</td>
<td>follicular adenocarcinoma</td>
<td>100% Intense</td>
</tr>
</tbody>
</table>
References

Are coroners’ necropsies necessary? A prospective study examining whether a “view and grant” system of death certification could be introduced into England and Wales

The paper by Rutty and colleagues’ fails to focus upon the key issues raised by the question it seeks to answer. Those issues are: (1) What is the “primary purpose” of coroners’ necropsies? (2) Is the “information available at the time of necropsy” adequate? (3) What is meant by postmortem examination? Does it only mean dissection of the whole body? (4) Under what circumstances should a necropsy be performed without regard to the views of the next of kin?

Figure 1 Expression of RANKL mRNA and protein in bone metastatic tumours. Signals are dark blue in colour. RANKL mRNA was present in the neoplastic cells of various metastatic tumours. Positive signals are brown in colour. RANKL protein was present at different intensities in the cytoplasm of the neoplastic cells of various metastatic tumours. All images are at x200 magnification. In addition, when present in surrounding tissues, osteoblasts and fibroblasts also expressed RANKL mRNA and protein (indicated by arrows). H&E, haematoxylin and eosin staining; ISH, in situ hybridisation; IHC, immunohistochemistry.
Androgen receptor expression in ductal carcinoma in situ of the breast: relation to oestrogen and progesterone receptors

We wish to add a reference to the list included in the paper of Selim and colleagues concerning androgen receptors in ductal carcinoma in situ (DCIS) of the breast that appeared in the Journal of Clinical Pathology in the first issue of 2002. Although the authors state that androgen receptors in DCIS have not been reported previously, we had studied this and published a paper dealing with our observations, in addition to CAG repeat lengths in the androgen receptor in DCIS.

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References

Authors’ reply
Thank you for this information and the opportunity to reply. Unfortunately, the study of androgen receptor (AR) CAG repeats by Kasami and colleagues is not included in the usual searches and this appears to be the reason for overlooking this reference. In this study, cases of fibroadenoma, ductal carcinoma in situ (DCIS), and invasive mammary carcinoma were included. Twenty-four cases of DCIS were tested for AR CAG repeats and 10 were tested for AR expression immunohistochemically. Two of 10 cases were positive for AR and these two cases were the only cases with apocrine morphology. However, in our study, we found that 19 of 57 cases of DCIS expressed AR. Thirteen of those 19 cases were not of non-apocrine morphology. In addition, of the nine morphologically apocrine cases, three lacked AR expression. It seems to be that AR is expressed in a subset of DCIS even without an apocrine morphology, but it is necessarily true that all morphologically apocrine cases of DCIS will express AR. In Kasami and colleagues’ study, none of the cases of invasive mammary carcinoma was tested for AR expression, but other studies have found that a subset of invasive breast carcinomas expresses AR. We feel that a study of AR CAG repeats in benign apocrine metaplasia, which is always immunohistochemically positive for AR, together with and without cases of apocrine and/or non-apocrine in situ and invasive breast carcinoma, would be very valuable in highlighting the importance of CAG repeats and apocrine differentiation.

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References

In our view, this last issue is the most important and other issues should be dealt with within that context: none of these issues can be dealt with meaningfully without informed public debate. The authors pay lip service only to this question and reach a conclusion “… we consider that necropsies still have an essential role within the coroner’s enquiry” that is self evident but superficial. The paper seems to be based on a false premise—that the “view and grant” facility could replace necropsies. In this study, the causes of death were predicted in 61–74% of cases; in Glasgow, view and grant is performed on approximately 10% of the deaths with which the department of forensic medicine is concerned. This procedure is regarded as an “alternative”, an adjunct to detailed review of the circumstances of death, allowing deaths where there is no suspicion or evidence of criminality to be certified without a necropsy.

The authors acknowledge that “the most important” factor in a pathologist’s ability to “predict a cause of death before necropsy” is “the quality of the information available to the pathologist”. However, there is no assessment of the quality of information provided in this study, despite a publication by one of the authors indicating the relatively poor quality of the information. A key question raised is: “Was there, in fact, no clinical information available or was the absence of information a reflection of inadequate enquiry on the part of the coroner?” The paper does not deal with that question but, sadly, ignores it with the following dismissive statement: “Any additional information concerning the deceased, which subsequently became available, was not included, because this could have caused bias in the second part of the assessment”. This appears to us a sad inversion of the importance of the issues.

The inference may be drawn from the paper that where adequate information was provided, allowing a prediction of cause of death, then “the number of correct predictions made of those where a cause of death had been proffered were as follows: A, 70%; B, 63%; C, 59%”. This appears to us to be the “true error rate”, reducing itself to 30–41%, as opposed to the authors’ preferred 54–61%; we would maintain that one should not include in any determination of “error rate” those cases where a prediction could not be made because of inadequate information: under the view and grant system a necropsy would have been carried out in such cases.

In a paper that attaches so much importance to accuracy of cause of death, it is doubly distressing to find a lack of precision in attributing death to “ischaemic heart disease” without further detail of the pathological basis for ischaemia and in finding “bronchopneumonia” an adequate explanation of death.

We think it unfortunate that this paper does not distinguish between the populations of “natural death” and “unnatural death” or give an indication as to whether any of those deaths that were considered to be natural before necropsy were shown to be unnatural—it is this distinction that appears to us to be the primary purpose of a system of investigation of death in which the wishes of the next of kin are irrelevant.

We welcome the opportunity afforded by the authors to add to the debate regarding the role and future of the coroner system. The authors’ implicit support for more detailed investigation of the circumstances of death before postmortem examination sits well with the “radical option”—foreshadowing a “medical examiner” system—detailed in the Home Office consultation document produced in the first phase of its Review of Death Certification, with recommendation 11—“the feasibility of establishing a new system of death certification involving a medical examiner should be explored”—in recent advice from the chief medical officer.

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References
Sensitivity to Quorn mycoprotein (*Fusarium venenatum*) in a mould allergic patient

S J Katona and E R Kaminski

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