

# Bone marrow biopsy morbidity: review of 2003

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**Background:** Although some hazards are recognised, in general, bone marrow aspiration and trephine biopsy are thought to be safe procedures. Until recently, no attempt had been made to quantify any attendant risks. For this reason, documentation of adverse events was begun in 2001, under the auspices of the British Society for Haematology. Three consecutive years have now been surveyed, the results for 2003 being presented here and compared with earlier results.

**Methods:** Members of the British Society of Haematology were requested to document adverse events associated with diagnostic bone marrow aspirates and trephine biopsies between 1 January and 31 December, 2003. Data were collected early in 2004.

**Results:** In total, 19 259 procedures were reported from 63 hospitals, 13 147 being combined procedures and 6112 aspirates without a trephine biopsy. Sixteen adverse events were reported, representing 0.08% of total reported procedures. The major adverse event was haemorrhage, which comprised 11 of the 16 adverse events. Although infrequent, adverse events were associated with significant morbidity and three were judged as very serious. The major risk factors for haemorrhage, in order of frequency, were diagnosis of a myeloproliferative disorder, aspirin treatment, other putative platelet dysfunctions, and thrombocytopenia.

**Conclusions:** Adverse events following trephine biopsies and bone marrow aspirates are rare, but nevertheless can have considerable impact on individual patients.

More than 20 000 bone marrow aspirates, with or without trephine biopsies, are probably carried out in the UK every year. Complications are rare, but until recent years have been poorly documented. In 2001, a patient died as a result of retroperitoneal haemorrhage after an aspirate and a trephine biopsy from the posterior iliac crest. Consideration of this tragic event led the British Society for Haematology to facilitate a national audit, which was partly retrospective for 2001 and prospective from 2002 onwards. In addition, some retrospective data for earlier years, necessarily less detailed because they dated back several decades, were also collected. The adverse events recorded in the first two surveys were analysed, were presented at the annual scientific meeting of the society, and have been published.<sup>1 2</sup> The data collected for 2003 have now been analysed, and can be aggregated with data from the previous surveys to permit firmer conclusions as to the frequency and nature of any complications and the risk factors for their occurrence.

"In 2001, a patient died as a result of retroperitoneal haemorrhage after an aspirate and a trephine biopsy from the posterior iliac crest"

## METHODS

Members of the British Society for Haematology were reminded late in 2002 that data for 2003 would be collected and that they should therefore prospectively record any misadventures associated with bone marrow biopsy procedures. A call for data to be submitted, using a proforma provided, was made early in 2004, with data being received mainly in the first three months of the year, but to a lesser extent during the subsequent three months.

## RESULTS

Data were submitted by haematologists from 63 hospitals. The total number of procedures reported was 19 259,

comprising 13 147 combined procedures and 6112 aspirates. The number of procedures for each hospital for each year varied from 65 to 1567, with a mean of 306 and a median of 216. The percentage of patients having a trephine biopsy varied widely, from 12% to 100%, with a median of 67% and a mean of 68%.

In total, 16 adverse events were reported, representing 0.08% of all reported procedures. The adverse events were largely haemorrhage (11), with other complications being infection (two), persistent pain (two), and a serous leak persisting for six days in a patient with non-Hodgkin lymphoma and nephrotic syndrome. One of the patients who suffered haemorrhage also had reduced mobility for four weeks and persisting pain for two months. There were three very serious events, all haemorrhagic in nature.

The bleeding episodes occurred particularly among those patients who had undergone a combined procedure, with only one of 11 instances occurring after an iliac crest aspiration alone. The haemorrhage was into the buttock and thigh in three patients, retroperitoneal in two, and not specified in six. Ten of 11 patients had risk factors for haemorrhage, often multiple. These are summarised and compared with previous years in table 1.

The three very serious events are described in detail. An obese patient with essential thrombocythaemia who was on warfarin for a mechanical prosthetic valve had had an international normalised ratio of 3.5 five days before the procedure; this was not re-checked on the day of a combined aspirate and trephine biopsy. Five days after the procedure he reported that he could not walk. He was found to have a haemorrhage into his thigh and buttock, with an associated fall of haemoglobin concentration from 150 to 101 g/litre. His international normalised ratio was 9.9 (he had been taking paracetamol and other analgesics). He was not transfused but required five days of hospitalisation. A second patient

**Abbreviations:** AML, acute myeloid leukaemia; MPD, myeloproliferative disorder

**Table 1** Risk factors for haemorrhage in patients who bled

	2003	Cumulative results from previous years	Total
Diagnosis of myeloproliferative disorder	5	13	18
Aspirin treatment	3	7	10
Warfarin treatment	1*	2†	3
Heparin treatment		1	1
Disseminated intravascular coagulation		2	2
Renal impairment		2	2
Von Willebrand's disease	1		1
Other putative platelet dysfunction	3 (2 AML, 1 MDS)	4 (3 MDS, 1 AML)	7
Thrombocytopenia	3 (platelet counts $6 \times 10^9/l$ in ITP and 39 and $86 \times 10^9/l$ in 2 patients with AML)	7 (platelet counts $17 \times 10^9/l$ in megaloblastic anaemia, $23 \times 10^9/l$ in AML, 25 and $68 \times 10^9/l$ in MDS, $38 \times 10^9/l$ post-BMT, and $96 \times 10^9/l$ in MPD)	7
Obesity	1	3	4

\*International normalised ratio (INR) between 3.5 and 9.9. †INRs 2.2 and 2.8.

AML, acute myeloid leukaemia; BMT, bone marrow transplantation; ITP, idiopathic (autoimmune) thrombocytopenic purpura; MDS, myelodysplastic syndrome; MPD myeloproliferative disorder.

had pain in the hip immediately after a combined procedure on the right posterior iliac crest. The pain persisted for three days and then spread to the right iliac fossa. She became acutely unwell, and was admitted to a high dependency unit with a retroperitoneal haemorrhage being shown on a computed tomography scan. She required inotrope and other circulatory support and high flow oxygen, but made a slow recovery without surgical intervention. Other than the diagnosis of a myeloproliferative disorder (MPD), there were no identifiable risk factors in this patient. The third very serious event was a retroperitoneal haemorrhage in a patient with no risk factors other than a diagnosis of chronic phase of chronic myeloid leukaemia. This haemorrhage led to blood transfusion, surgical drainage, postoperative ventilatory support and 11 days of hospitalisation, with slow wound healing over three to four weeks.

In addition to the three patients regarded as having suffered a very serious event, there were two patients with haemorrhage who required transfusion of red blood cells (one of whom had blood tracking down to the ankle with a 20 g/litre fall in haemoglobin concentration) and two who required platelet transfusion. Two of these patients had a hospital stay prolonged by one or two days.

In comparison with the haemorrhagic episodes, other complications were less serious. Two patients had persistent pain for several weeks. Two others, one with acute myeloid leukaemia (AML) and one with a poor prognosis myelodysplastic syndrome, developed local infection that responded readily to treatment. The patient with AML was obese and the procedure was difficult. The patient with nephrotic syndrome who suffered a serous leak required six days of hospitalisation with pressure dressings.

During 2003, in contrast to earlier years, there were no adverse events relating to breaking of needles.

In previous years, data have suggested that adverse events may be somewhat more likely with less experienced operators. This was not substantiated by the current data. Only a single procedure of the 11 biopsies that were followed by haemorrhage had been carried out by a senior house officer and that person had had a year's experience. Most were carried out by staff grade or consultant haematologists who had had 10 to 20 years experience, and in some cases had performed more than a thousand procedures.

## DISCUSSION

The findings in 2003 have confirmed those of earlier years in identifying a diagnosis of MPD as a risk factor for haemorrhage. The MPDs involved were mainly essential thrombocythaemia (three of five cases in 2003 and seven of 13 in previous years), but also included polycythaemia vera,

chronic myeloid leukaemia, and idiopathic myelofibrosis. Many of these patients were not taking aspirin or other platelet antagonist, so the risk appears to relate at least in part to the primary diagnosis, rather than to antithrombotic treatment. Other risk factors identified in more than occasional patients were aspirin, thrombocytopenia, and putative platelet dysfunction, with or without thrombocytopenia (in patients with AML or myelodysplastic syndrome). For the first time in 2003, a significant haemorrhage was reported in a patient with autoimmune thrombocytopenic purpura, but given that this is the first such report in three years this must be regarded as a rare event. Heparin and warfarin can clearly be associated with major haemorrhage, but this is relatively uncommon, probably because haematologists are becoming increasingly cautious about performing biopsies in anticoagulated patients. The single serious haemorrhage reported in association with warfarin during 2003 has already led to a review of procedures and to stricter guidelines in the hospital concerned.

Haematologists need to be aware of the various ways of minimising risks and of dealing with adverse events when they occur. It has been suggested that when obesity presents a problem, bone marrow biopsy procedures should be performed under computed tomography control.<sup>3</sup> The data from these surveys suggest that retroperitoneal haemorrhage may be more hazardous than haemorrhage into the buttock and thigh, possibly because the diagnosis is more likely to be delayed and management may therefore be less adequate. If a patient is unfortunate enough to suffer a retroperitoneal haemorrhage, embolisation of a bleeding vessel may obviate the need for hazardous surgery.<sup>4</sup>

*"Haematologists need to be aware of the various ways of minimising risks and of dealing with adverse events when they occur"*

Infection is uncommon and generally less serious than haemorrhage. Neutropenia and defective neutrophil function may be risk factors because the two instances of infection in 2003 were in patients with myeloid neoplasms (AML and MDS).

Overall, complications were much less often reported in patients with lymphoproliferative disorders than in those with myeloid neoplasms, possibly because the latter are more likely to have neutropenia, thrombocytopenia, and defective neutrophil and platelet function.

The surveys carried out to date have given useful information that has served to maintain awareness of the

### Take home messages

- In a review by the members of the British Society of Haematology of adverse events associated with diagnostic bone marrow aspirates and trephine biopsies in 2003, such events were reported in 0.08% of total procedures
- The major adverse event was haemorrhage (11 of the 16 adverse events)
- Although infrequent, adverse events were associated with significant morbidity, and three were judged as very serious
- The major risk factors for haemorrhage, in order of frequency, were diagnosis of a myeloproliferative disorder, aspirin treatment, other putative platelet dysfunction, and thrombocytopenia
- Thus, although adverse events after trephine biopsies and bone marrow aspirates are rare, they can have considerable impact on individual patients

possibility of an adverse outcome from a bone marrow biopsy. It is also possible that the annual presentation of results of this ongoing survey has served to remind haematologists that adverse events, although rare, are nevertheless important and steps must therefore be taken to minimise their occurrence. It is therefore planned that annual surveys should be continued.

### ACKNOWLEDGEMENTS

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