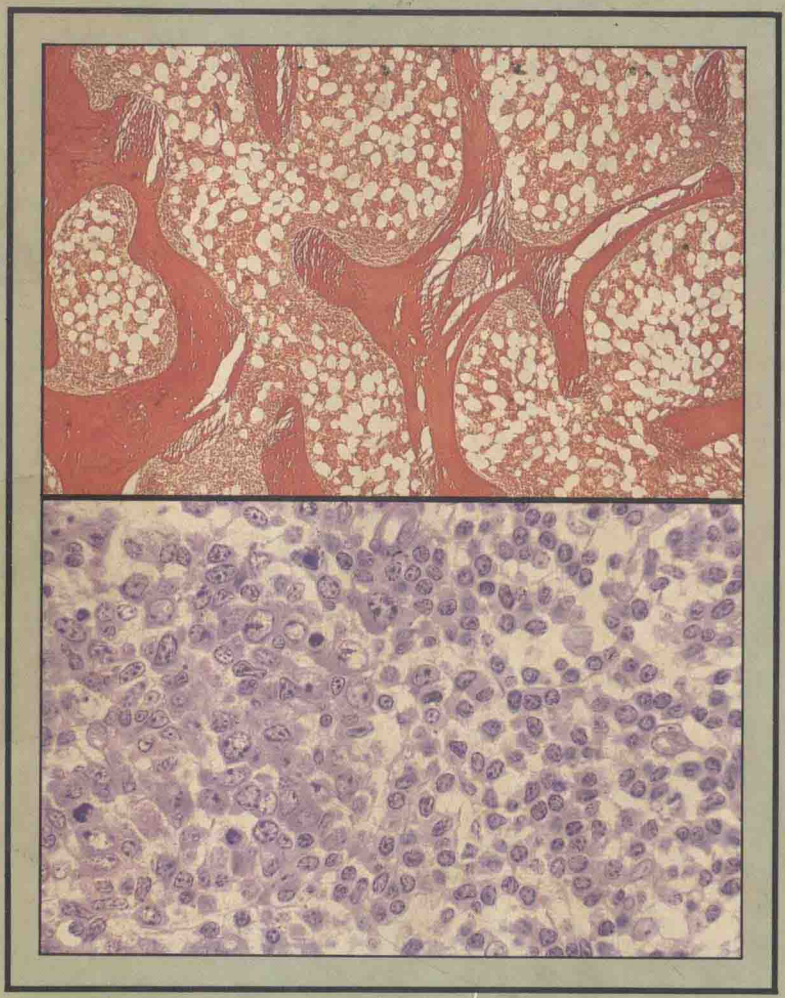
Biopsy Pathology of Bone and Bone Marrow

B. Frisch, S.M. Lewis, R. Burkhardt and R. Bartl

Biopsy Pathology Series



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To Professor U. Seligsohn
in appreciation of his encouragement
B.F.

Preface

Morphology has been the basis of haematology from the very beginning of this clinical and scientific discipline. Bone marrow aspiration by means of needle puncture has provided material for recognizing abnormal haematopoietic cells and for diagnosing blood diseases for over 50 years since M. J. Arinkin described (in *Folia Haematologica*, **38,** 233, 1929) the method for needle aspiration of the bone marrow. Smears made from aspirated samples and stained by one of the Romanowsky staining combinations provide excellent cytomorphological detail. However, because the distribution of haematopoietic cells differs from one area to another in the marrow, aspiration does not always reflect true distribution of cells in the marrow; nor will an aspiration demonstrate the spatial relationships of haematopoietic cells and their precursors within the marrow framework; nor the extent of marrow involvement in lymphomas and other malignant diseases, nor the effect of intramedullary diseases on bone, and that of osseous condition on the marrow.

Marrow biopsy by surgical trephine is an older procedure than needle aspiration; the earliest published reports of this technique include those of Pianese in 1903 who obtained marrow from the epiphyses of the femur and Ghedini in 1908 who trephined the upper third of the tibia. Subsequent workers developed the technique of trephine biopsy from sternum and from iliac crest. This became established as a diagnostic procedure to supplement a bone marrow puncture in haematological diagnosis. But the ease of aspiration contrasted with the difficulty in obtaining adequate material for sectioning, and the laborious procedure for preparing sections was hardly justified by the end product. Whilst the technique was helped by improved needle and trephine design, sections of decalcified biopsies remained a poor substitute for aspirated material in studying cell morphology.

In the past decade major changes have taken place—new needles have been developed ensuring that the biopsy can be carried out with little discomfort to the patient and with little or no damage to the biopsied

tissue. Finally, methods of plastic embedding, largely pioneered by one of us (RB) enable the preparation of semi-thin and undecalcified sections of bone marrow which can then be stained to reveal cytological features in detail equal to that obtained with smeared cells, but without the artefact of the smearing. This has opened up a new field for investigating the pathophysiology of the bone and the bone marrow.

Traditionally, interpretation of bone marrow aspirates has been the responsibility of the haematologist whilst interpretation of sections has been the responsibility of the histopathologist who is equally concerned with the histology of the adjacent bone; but bone and bone marrow are intertwined tissues and the expression of their interdependence in practically every disease affecting either one or the other, has only recently been recognized. In addition biopsy is becoming an important tool for exploring the pathogenesis of cancer metastases, angiogenic and endothelial cell factors, the stimulus of cytotoxicity and other fundamental aspects of cellular biology. For essential diagnostic purposes and for the studies mentioned above, bone biopsy has become a procedure of importance equally to the haematologist and the histopathologist as well as to the general physician.

There are a relatively large number of atlases on blood cell morphology which amply illustrate the haematopoietic cells of the bone marrow. Conversely, there have been few atlases or textbooks dealing exclusively with the histological morphology of bone and bone marrow biopsies; our intention was to provide a comprehensive textbook illustrating the features which are likely to be encountered in trephine biopsies in various conditions, and to supplement the descriptive text with an outline of the pathophysiology based on the morphological features.

The nature of the subject requires illustrations and we hope that we have provided these in sufficient abundance to serve a useful purpose. The monochrome figures have been supplemented by 16 colour plates. The cost of these have been partly offset by a generous grant from the Gesellschaft für Strahlen- und Umweltforschung mbH, München.

This has enabled the publishers to keep the price of the book lower than would otherwise have been possible; for this and for invaluable editorial help we are grateful to Dr Peter Altman and Chapman and Hall Ltd. The authors would also like to express their gratitude to all colleagues who referred patients or sent biopsies, to the technical staff of the laboratories in which the work was undertaken and the photographic units where the photomicrographs and sketches were prepared. This work was supported by the Gesellschaft für Strahlen- und Umweltforschung mbH, Munich.

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Contents

1 Introduction

In recent years the indications for bone marrow biopsy (BMB) have broadened, so that they are now employed in the investigation of many disorders in haematology, internal medicine, oncology and osteology (Burkhardt, 1971; Byers, 1977; Krause, 1981; Gruber *et al.*, 1981; Westerman, 1981; Burkhardt *et al.*, 1982; Rowden *et al.*, 1982; Bartl *et al.*, 1982). The upsurge of interest was spurred by improvements in instrumentation for taking BMB (Burkhardt, 1971; Jamshidi and Swaim, 1971) as well as in processing the undecalcified cores into plastic embedding media, thus providing optimal histology for evaluation in the light microscope (TeVelde *et al.*, 1977; Brinn, 1979; Takamiya *et al.*, 1980; Burkhardt, 1981; Westen *et al.*, 1981; Beckstead *et al.*, 1981; Moosavi *et al.*, 1981; Block *et al.*, 1982; Frisch *et al.*, 1982).

There have been previous atlases and textbooks describing results with wax-embedded biopsies (e.g. Krause, 1981). But because of the advantages of plastic embedding (and also because this technique is rapidly being adopted in many centres), this book is based on the results of biopsies embedded without decalcification. Moreover this book deals strictly with diagnosis of bone marrow histology, with the emphasis on the findings in iliac crest biopsies, as these are clinically the most widely used.

A list of biopsy instruments, description of the techniques for taking them, a method for the rapid processing of the biopsy cores and the most commonly used staining methods are given in the Appendix.

In view of the large number of papers on BMB which have appeared in the literature in the last few years since the early publications of Burkhardt (1971), Duhamel (1974), Block (1976), and Rywlin (1976) only recent review articles will be cited as far as possible. In addition, this book relies heavily on observations made in the authors' laboratories on over 30 000 biopsies. Due to the limitation of space, and because this is intended principally to be a diagnostic text for bone marrow histopathology, some conditions in which a bone biopsy is unlikely to be performed, have been omitted.

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1.1 Patients

Bone marrow biopsies may be taken from patients at all ages from birth onwards. Specially designed needles are available for babies and very young children. Informed consent is obtained from the patients after the procedure has been fully explained, or from either parents or guardians if the patients are under the legal age for consent.

1.2 Biopsy sites

The anterior and the posterior iliac crests are the preferred sites from which the biopsies are taken after local anaesthesia (see p. 281). This does not apply to biopsies taken under radiological guidance (Burkhalter *et al.*, 1983) or surgical biopsies obtained under general anaesthesia in the operating theatre, when the site depends on the diagnostic requirements and the surgeon's choice. There are differences in the amounts of trabecular bone and marrow in different regions of the ilium, but these have no practical significance (Whitehouse, 1977; Whitehouse *et al.*, 1971). Likewise, the proportions of bone, parenchyme and fat vary in the different parts of the skeleton containing the red haematopoietic marrow, but the basic constituents are the same (Wintrobe, 1981; Trubowitz and Davies, 1982). For example, the volume percentages of trabecular bone are less, and those of the marrow cavities are greater in sternum and vertebral bodies, than in the ilium, and they also have a higher parenchyme to fat ratio, (a factor contributing to the popularity of the sternum as a site for aspiration).

1.2.1 Contra-indications and complications

Bone biopsies are (relatively) contra-indicated in patients with bleeding disorders; if absolutely necessary, the same precautionary measures must be taken as for other operations in such patients. Infections occur rarely, about once in a thousand biopsies (see also Appendix, p. 282).

1.3 Biopsy instruments

There are two main groups of instruments, namely electric drill and manual trephines, various types of which are on the market (see Appendix). The drill is used for vertical, and the wide-bore manual trephine for horizontal trans-ilial biopsies—both provide relatively wide cylinders (4 mm and 8 mm respectively), and are recommended when histo-morphometric measurements of cortical and trabecular bone are envisaged.

However, in most cases the 11 or 8 gauge trephines (2 or 3 mm width) are employed and the biopsies are taken from the superior spinous process of the posterior iliac crest. The length of these biopsies varies, but may reach 3–4 cm (details for the use of the different instruments are given in the Appendix). Representative sections of biopsies taken with the various needles are shown in Figs. 1.1 and 1.2.

In a retrospective series of 15 000 biopsies taken with the electric drill,

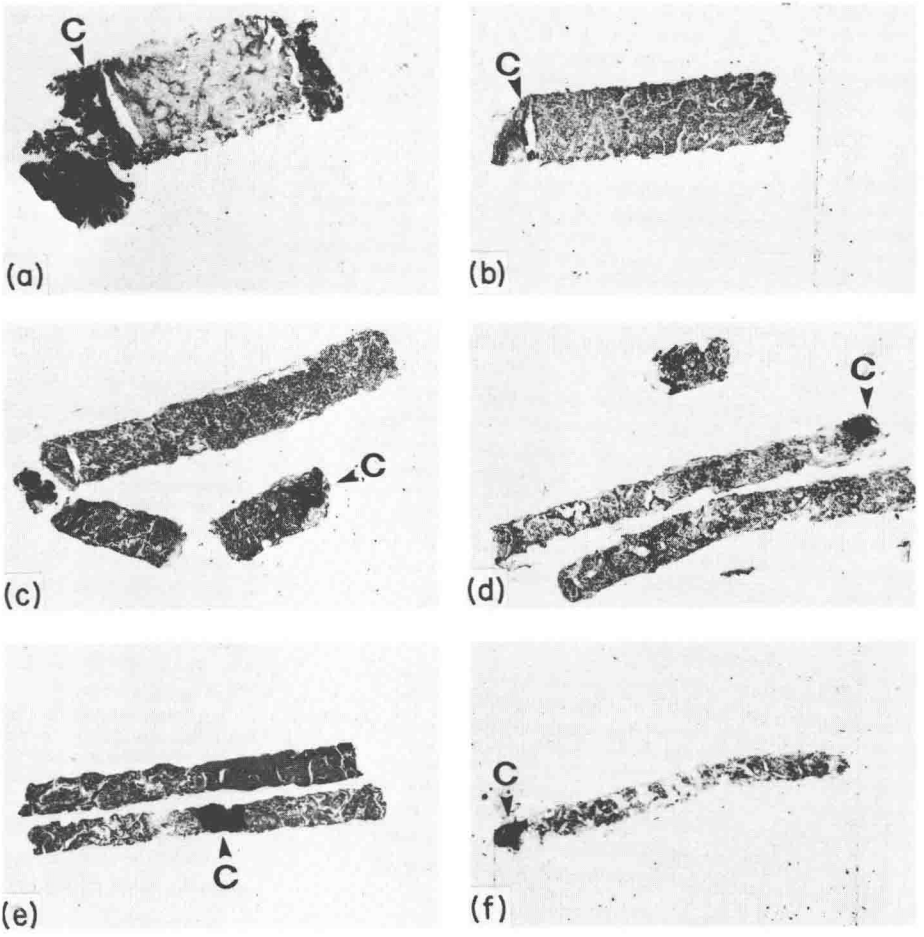

Fig. 1.1 Examples of bone biopsies taken with different instruments, all photographed at the same magnification. Actual sizes: (a) transilial 7 × 18 mm; (b) myelotomy drill 4 × 17 mm; (c) disposable regular bore 2 × 20, 2 × 22 mm; (d) Islam needle 2 × 22 mm; (e) Islam needle 2 × 25 mm; (f) Jamshidi, regular bore 1.5 × 21 mm. c = cortex.

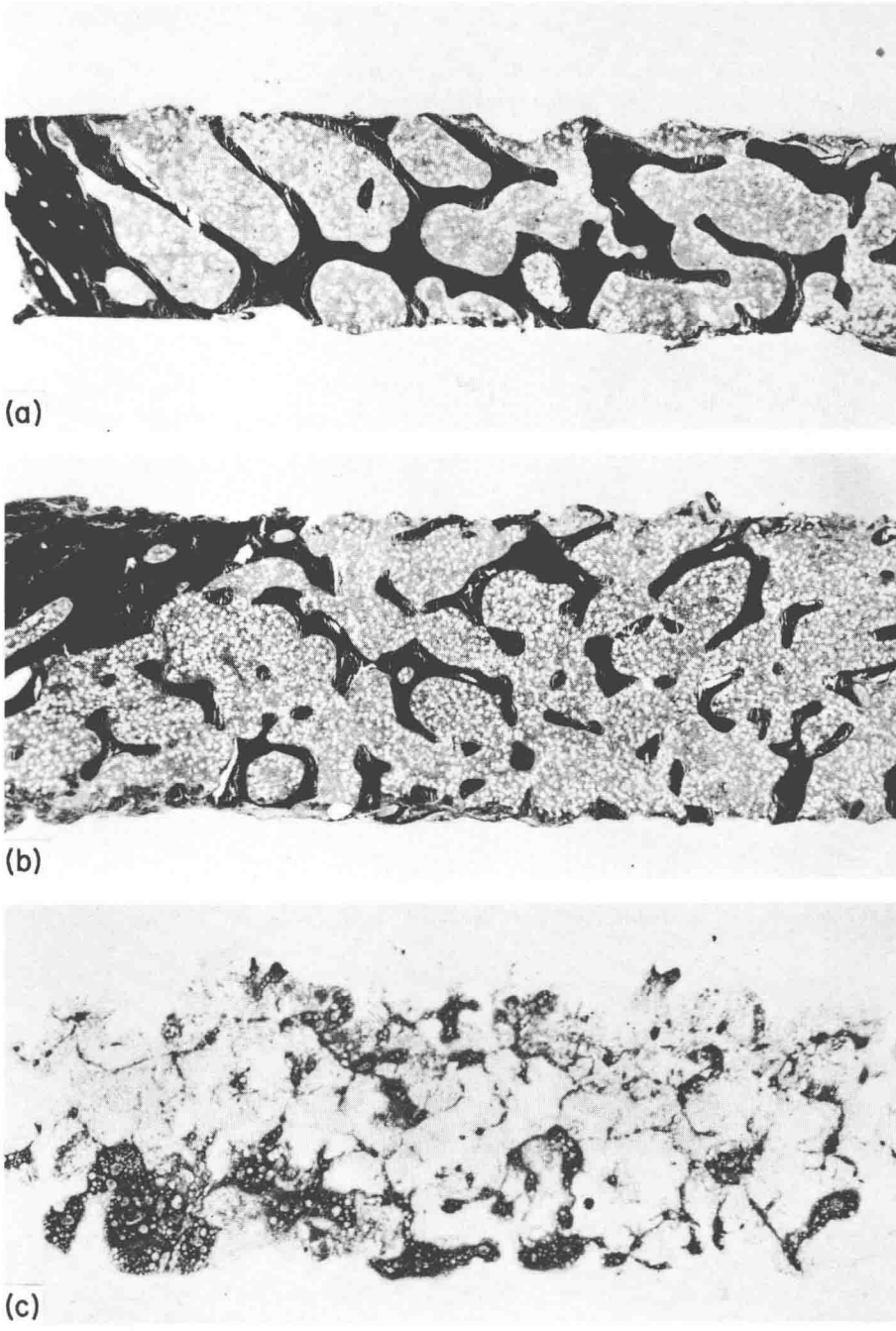

Fig. 1.2 Section of biopsy taken (a) with the Jamshidi needle. × 10, Gomori; (b) with the electric drill. × 10, Gomori; (c) biopsy imprint. × 10, Giemsa.

about 1% were inadequate; and about 10% of 18 000 taken with the Jamshidi needle. However, with the recent modifications and new models of the manual trephines, the results with both methods are comparable.

Scintigraphic investigation of the ilium after bone biopsies revealed no abnormalities when the biopsies had been taken with the manual trephines (Tyler and Powers, 1982). Previous studies on biopsies taken from the sternum, the thoracic and lumbar vertebrae and the iliac crest, have demonstrated that the iliac crest biopsy may be regarded as representative of the haematopoietic marrow, though there are quantitative differences in the amount of bone present (Whitehouse, 1977; Bartl *et al.*, 1982).

1.4 Indications

A long list of indications has now been established in haematology, internal medicine, oncology and osteology; it can be summarized as follows:

(1) In all cases in which aspiration of the bone marrow is considered as a diagnostic procedure there are advantages in taking a biopsy at the same time. The patient is psychologically prepared, the local anaesthetic will have been administered, and the mental and physical stress of another procedure later on will be avoided. Moreover, since aspiration and biopsy are complementary procedures, if the biopsy is omitted, the physician does not get the maximum information and therefore the patient does not have the full benefit of the investigation.

(2) In all conditions that might affect the bone, either primarily or secondarily.

(3) Clarification of numerous other disorders, such as infections, including toxo- and histoplasmosis (Jones and Goodwin, 1981), granulomatous conditions, amyloidosis, vascular disease, pyrexia of unknown origin, and the effects of metabolic disturbances (Kass, 1979; Krause, 1981; Frisch *et al.*, 1982).

(4) Whenever a dry tap or insufficient material is obtained on aspiration.

(5) In all patients with suspected or clinically established myelo- and lymphoproliferative disorders, other malignancies, myelodysplastic states, cytopenias, storage diseases and assessments of haematopoietic tissue for whatever reason (Burkhardt *et al.*, 1982; Bartl *et al.*, 1982; Frisch *et al.*, 1982).

(6) For monitoring of therapy or the evolution of the disease process, detection of residual foci of malignant cells; for assessment of the marrow