Light microscopy of macerated (dry) bones was first practised routinely at the end of the 19th century. The first publications dealing with the microscopic structure of fossil bones (e.g., Schaffer 1889) also appeared around this time. Microscopy has been used in paleopathology since the 1920s. Initially, when paleohistology [this term was introduced into Anglo-Saxon literature by Moodie (1923)] started to develop, the samples were decalcified, embedded in paraffin wax, and cut by microtome, or polished surfaces of undecalcified bone were examined using normal (plane) and polarized light. Short reviews on the early years of paleohistology and paleohistopathology have been given by Garland (1993), Martin (1991), Ricqlès (1993), and Stout (1978). Moodie (1923) published very informative photomicrographs that demonstrated specific structures in fossil, and prehistoric animal and human bones, and Weber (1927) examined prehistoric human long bones to diagnose treponemal diseases.

Archeological bones are very brittle and, as a rule, they cannot be decalcified to be sectioned by microtomes without destruction of the sample. Thus, ground sections and new techniques of embedding gradually, became the methods of choice. From the 1950s on Ascenzi (1969), Baud and Morgenthaler (1956), Hackett (1976), Ortner (1976a), Stout (1976) and Stout and Simmons (1979) have carried out important research in the field of paleohistopathology of dry bones mainly using ground sections. More recently, particularly in North America, paleohistopathological research using light microscopy has been carried out mainly in connection with histological morphometrics of compact bone and measurements of bone formation rates (e.g., Frost and Wu 1967; Martin and Armelagos 1979, 1985; Richman et al. 1979; Pfeiffer and King 1981; Weinstein et al. 1981).

Interestingly, the investigation of mummified tissues was more popular at the beginning of paleohistopathology (e.g., Ruffer 1911; Williams 1927; Wilson 1927). Later, after World War II, scientists like Sandison (1957), who was one of the leading authorities, carried out paleopathological research on ancient mummified tissues at the microscopic level. Although the histology of mummified soft tissues has been investigated relatively frequently (e.g., Brothwell et al. 1969; Sandison 1970; Cockburn and Cockburn 1980; Zimmerman and Kelley 1982), the histopathology of archeological bones was rarely a subject of interest (e.g., Lagier and Baud 1980; Kramar et al. 1983).

**THE NEED FOR MICROSCOPIC ANALYSIS**

Microscopic analysis in paleopathology leads both to diagnoses of ancient diseases and to improved age determinations (e.g., Kerley 1965; Kerley and Ubelaker 1978; Schultz 1986; Stout 1992; Wolf 1999). Additionally, microlevel investigations can detect changes, such as inactivity atrophy, which are not clearly observable macroscopically (Schultz 1986, 1997b). Also, the effects of heat and fire that occurred perimortem or postmortem lead to typical changes in the microstructure of bones (Grimm and Strauch 1959; Teschler-Nicola and Schultz 1984; Schultz 1986, 1997b; Piepenbrink and Herrmann 1988). In the case of small bone fragments, whether they are human or animal may be unclear. The histological analysis of a bone sample can establish their identity (Harsányi 1978, 1993). Furthermore, microscopic investigation of archeological bone samples can frequently yield important clues as to the state of...
preservation and the kind of postmortem destruction (e.g., Stout and Teitelbaum 1976; Hackett 1981; Schultz 1986, 1994b, 1997b), which are necessary data for dating archaeological bones by radiocarbon techniques, or for molecular work, for instance, on ancient DNA and collagenous and noncollagenous bone proteins, or examination of trace elements and stable isotopes (Schultz 1986, 1997b).

Reliable diagnosis is the basis of etiology and epidemiology of diseases in ancient populations. However, this is not always easy. As a rule, paleopathologists can examine only the vestiges of ancient diseases in dry bones; there are no soft tissues or cells, which play an important role in pathological investigations on recent materials, to be studied to establish a reliable diagnosis or for comparative purposes. Therefore, cytological examinations cannot be undertaken and only a limited histological examination is possible. When archeological bone remains are studied by macroscopy alone or even additionally by radiological techniques such as conventional x-ray images and computed tomography (CT) scans, the rate of false diagnoses is still high. However, the microscopic investigation of thin ground sections produces even more reliable results than the use of multislice CT (MSCT) which is an advanced form of helical computed tomography (Rühli et al. 2000, 2001). All this means that diagnostic criteria are sometimes relatively limited in paleopathology. Therefore, special methods and techniques, particularly at the microscopic level, need to be established to render such diagnoses more reliable (Schultz 2001b).

Light microscopy (particularly with polarized light), microradiography, and scanning-electron microscopy are so important for differential diagnosis of dry bones that they can no longer be neglected (Schultz 2001b). Whereas several reliable techniques are now available (Schultz and Drommer 1983; Schultz 1988), paleopathologists would be well advised to employ these useful tools. Many bone changes that cannot be observed by macroscopic analysis are revealed by microscopic techniques (Schultz 1988), and many alterations caused intravitam by disease can clearly be differentiated from changes due to postmortem reactions (Schultz 1986, 1994a, 1997b). The nature of bone tumors and tumorous lesions (Figures 6-1; cf. 6-12) can be detected microscopically, as can the different structures that occur as a result of specific and nonspecific bone inflammations (Hackett 1976; Schultz 1986, 1999a; Schultz and Teschler-Nicola 1987b; Schultz and Roberts 2002, in press). Also, changes caused by metabolic diseases, processes of aging, and decrease or increase in physical activity are identifiable with the aid of microscopic methods (Schultz 1986, 2001a), and initial stages of bone diseases that are not visible by macroscopic examination can be clarified by microscopic techniques. Particular diseases cause typical unmistakable lesions in the bone matrix (Schultz 1993b). The contribution of microscopic investigation of dry bone specimens to our knowledge of differential diagnoses and the development of diseases is demonstrated by the classical article on treponematoses written by Hackett (1976). This chapter contains figures that clearly describe the different stages of bony destruction in the skeletons of people suffering from yaws and venereal syphilis. The basis for elucidation of these stages lay in Cecil Hackett's long years of experience with the histopathology of dry bones.

Finally, the impact of microscopic research on the field of epidemiology of diseases in ancient populations can also be illustrated (Schultz 1993b). In the Early Bronze Age population from Ikiztepe, northern Anatolia, 144 infant and child burials were available for paleopathological investigation. Of these, 129 individuals with preserved skulls were suitable for the study of anemia, rickets, or osteomyelitis and 117 individuals with preserved skulls were suitable for the study of meningeal irritations (Schultz 1990). The
MATERIALS AND METHODS

The majority of samples examined in paleohistopathology are subfossil skeletal remains of human beings and other animals and, only occasionally, fossil remains (Schultz 1999c). The extent to which microscopic analysis, particularly histology, can contribute toward establishing a reliable diagnosis depends on the state of preservation (Schultz 1997b). Sometimes, preservation is so poor that it is impossible to obtain a convincing age determination or a disease diagnosis using macroscopic methods alone and we have no choice but to attempt a microscopic investigation. In very extreme situations, only the outline of the skeleton, a leichenschatten, is preserved. Even then, microscopic analysis of the earth that contains very small bone fragments can sometimes give a satisfactory result (Schultz 1997b). In contrast to the examination of skeletal remains, mummified tissues have been investigated only occasionally. Microscopic studies of bog corpses are rare (Fischer 1981; Piepenbrink and Herrmann 1988; Schultz 1988).

In addition to the macroscopic examination of archaeological skeletal remains, it is worthwhile to inspect all bone surfaces with a magnifying glass because, sometimes, very inobtrusive vestiges can be recognized. Stereoscopic low power microscopes allow further studies. These methods are not invasive, which is a great advantage because nothing is damaged. The disadvantage is that no information about the internal structure and the composition of newly formed bone, such as a secondary layer on the original bone surface, can be gathered.

After a long bone has been sawed to obtain a sample for microscopy, the cut should be inspected very carefully because often there is information, such as form, distribution, and nature of growth of the newly built bone, that could be important for the diagnosis. As mentioned already, the ground section should include, if possible, a complete cross section of the bone, for instance, the shaft of a femur. Otherwise, the necessary information is reduced and a reliable diagnosis might not be possible. There is a false assumption that paleohistopathologists only need a very small bone sample for their study (the smaller the better) because they are working at the microlevel. This assumption is incorrect. It is necessary to examine not only a small area of the
affected bone, but also the interface between diseased and nondiseased bone tissues. In this way, the nature of pathological bone growth as well as the changing quality of the bone tissues (e.g., different kinds of woven and lamellar bone) can be studied. This means that for a histopathological investigation, at least one or even better, several adequate samples from the diseased bone have to be taken.

To obtain a reliable diagnosis, it is important to prepare at least two thin ground sections from different levels from each sample taken from a bone (cf. Figure 6-32) because microscopic structures can also change in their three-dimensional architecture. After collection of specimens, the gaps in the bone can be supplemented by plaster or a cast so that the original macroscopic appearance is restored.

Thus, researchers should make use of a variety of techniques, especially microscopic techniques, that help to establish a reliable differential diagnosis, when they are studying not only case reports, but also the etiology and epidemiology of ancient diseases.

Light microscopy can be employed in two ways. Polished surfaces of bone samples can be observed using reflected light or ground sections can be examined by transmission light. For the latter method, which is much more efficient, the bone sample has to be sectioned or ground down to make it translucent. For archeological or sometimes even forensic bones, the method of choice is the grinding process (e.g., Hackett 1976; Stout 1992). I have modified these techniques (Schultz 1988; Schultz and Drommer 1983) by using a special embedding procedure that permits the preparation of thin ground sections with a thickness ranging between 15 and 100 μm. The nature of pathological structures can then be detected relatively easily (Moodie 1923; Weber 1927; Michaelis 1930; Hackett 1976; Schultz 1986, 1987b, 1993a, b; Blondiaux et al. 1994). Although light microscopy is a relatively old technique, it remains the most efficient, whereas with regular scanning-electron microscopy only the surfaces of a bone or the cut or sawed planes of bone sections can be checked as described for the examination by stereoscopic low power microscopy.

Excavated skeletal remains are usually fragile and extremely brittle, and no longer have the quality of fresh bone. Archeological undecalcified bone, embedded or not, should never be cut by microtome, because the procedure can cause serious artifacts (e.g., microfractures, decay) that lead to false diagnoses. Decalcified bone is easier to cut. However, if a poorly preserved bone sample is decalcified, nothing much remains that is worth analyzing and special techniques must be used to sample and prepare histological specimens (Kaissling 1973; Donath 1983; Schultz and Drommer 1983; Schultz and Brandt 1987; Schultz 1988, 1997a). For the latter, the technique of choice is the preparation of undecalcified thin ground sections, which is highly suitable even for very poorly preserved bone samples.

To prepare thin ground sections for light microscopy, a special technique was established based on the method of plastination developed by Hagens (1979) and modified for histological purposes by Schultz and Brandt (cf. Schultz 1988). The embedding medium is a special epoxy resin and prior to embedding, the samples are dehydrated using ascending concentration steps of alcohol solutions (e.g., solutions of 40, 50, 60, 75, 80, 85, 90, and 95% of alcohol, usually for one day each). The last step is immersion in methyl chloride as an intermediate solution for the exchange of substances. The sample is then ready to be embedded. Our decades of experience have shown that the most suitable embedding substance for macerated bone samples is the epoxy resin Biodur®, which was developed by Gunther von Hagens (cf. Hagens 1979). Biodur® is easy to handle during the embedding procedure, which takes place under a relative vacuum (motor vacuum pump). This resin is highly suitable for organic materials that may still contain minimal vestiges of moisture. Using Biodur®, the embedding process takes at least three weeks, but, the results are excellent. Thus, the whole process, from sawing a sample from a bone until the moment when the thin ground section is viewed under a microscope, can take four to six weeks. The embedded samples are mounted on a glass slide, cut with a special circular saw (Dr. Steeg und Reuter, Frankfurt am Main), and ground down to a thickness of 100 μm (for micrographs), 70 μm and 50 μm (for unstained thin ground sections examined in plane or polarized light), or 15 μm (for stained thin ground sections examined for cells, collagen bundles, and special soft tissue structures in plane light) with the same saw using a special circular disk. Finally, the polished ground section is labeled and protected by a thin cover glass. Specimens prepared by this procedure, even from brittle or rotted bone, can be examined satisfactorily and no artifacts are produced by the embedding. (The use of methyl methacrylate or the grinding process, for instance, can sometimes disturb the microscopic examination of even large specimens.)

A final point in the assessment of possible techniques is the following. A microtome section of an undecalcified bone sample is, as a rule, small (i.e., 5 x 5 or even 10 x 10 mm). With a Leica sawing microtome (Innenlochsäge), the sample size is larger (ca. 25 x 25 mm). However, for thin ground sections prepared after the plastination process from an undecalcified bone sample, the sizes of the sections for routine examinations can be 28 x 48 to 46 x 76 mm or, in special cases, even larger (e.g., 120 x 120 mm). Thus, using the latter technique, a cross section of a femur can be examined in its entirety in the same section, even if the bone is thickened to double or triple its size by osteomyelitis. Diagnosis criteria for macerated bone samples differ from the criteria used in recent pathology and large samples of bones, such as complete cross sections, are inevitably necessary. Large sections from undecalcified bone samples can be prepared only after embedding the sample because, as
we have seen, archeological bone is, as a rule, very brittle and sometimes even degraded.

The use of transmission microscopy in plane and polarized light allows unstained and stained thin ground sections of hard tissues (e.g., from bone samples) as well as unstained and stained sections of soft tissues (e.g., from muscles, liver, lungs) prepared by microtome to be investigated. In particular, stained sections made from soft tissues are very clearly observable in plane light.

Several techniques are available for preparation of histological sections from mummified soft tissues for microscopic research (e.g., Sandison 1955). All of these techniques are based on rehydration of the mummified samples before cutting with a microtome. Sometimes the process of rehydration considerably damages or even destroys the original connection between the different tissues, particularly the connective tissue, because of the relative swelling of the tissues and because small parasites that affected the individual during his or her lifetime can be washed out by the rehydration process (Schultz and Gessler-Löhr 1992).

Therefore, a new technique for preparing histological specimens of mummified tissues using thin ground sections was introduced. A very efficient procedure for preparing thin ground sections of prehistoric and historic skeletal remains recovered in archeological excavations or kept in bone collections has already been described (Schultz and Drommer 1983; Schultz 1988), but this technique has never been used for mummified soft tissues. The idea is that soft tissue samples are embedded without rehydration using a modified plastination process (Schultz and Gessler-Löhr 1992; Schultz 1997b). This embedding technique was used to prepare thin ground sections from soft tissues of an organ bundle from an old Egyptian mummy of a boy who died at the age of 5–7 years. The thin ground sections showed many very small parasites, which were identified as *Microfilariae*, that were still in place in the soft tissue and indicated that the boy suffered from *Microfilariaiasis* (Schultz and Gessler-Löhr 1992). No *Microfilariae* were found in rehydrated samples. There are many other cases where this technique worked sufficiently well, for instance, to study the debris of arthropods in canals in mummified tissues (Schultz 1993b).

The use of polarized-light microscopy is good for examining ground sections produced from dry bone samples. The identification of collagen fibers and the special pattern of mineralized structures in normal and pathologically changed bones, as well as in calcified and ossified soft tissues, for instance, parts of blood vessels, tendons, muscles, and meninges, can easily be carried out using polarized light. Thus, structural changes caused by pathological processes can be classified. Also, various crystalline substances (e.g., cholesterol and uric acid), which are, for instance, found in gallstones and renal calculi, can be detected and classified (cf. Schultz 1982). Undecalcified archeological bone samples cut by microtome (i.e., not a ground section) can, of course, also be studied in polarized light. However, the result is unsatisfactory and frequently leads to false diagnoses because of the artifacts produced by the cutting procedure (e.g., microfractures). The examination of decalcified bone samples in polarized light is, as a rule, also highly unsatisfactory, because the decalcification procedure apparently affects not only the apatite but also the collagen structure.

Polarization microscopy is also used in the field of paleontology and paleoanthropology to study the microstructure of fossil bone (e.g., Schultz 1999c) as well as in forensic anthropology to estimate the time a skeleton has remained in the soil. This latter can be achieved using quantitative methods (Berg 1982, 1997). Another, relatively rapid method in which some of the undecalcified bone tissue is filed off, was developed by Berg (1982). The bone dust is stirred and then quantitatively examined in polarized light to determine the amount of anisotropic particles. This method, however, provides only a very rough estimation of burial time.

The use of a red first order (quartz) hilfsobject as a compensator in the light path of the microscope (Schultz 1988) yields more information on the features of macerated bone and ossified soft tissues because various structures (e.g., collagen fibers in poorly preserved bone structure and their orientation as well as agents and products of diagenesis, such as crystals, and floral and faunal remains) are more easily observed. Additionally, an impression of the three-dimensional structures of bone can be gained. Using such a hilfsobject as a compensator, the microscopic view of an unstained, 50 μm thick thin ground section becomes very colorful in polarized light due to the physical phenomenon of interference (cf. Schultz 2001b) between the crossed polarizing filters (Nikols). The background is always a light purple–red. The course of collagen fibers (e.g., in the haversian systems) has the same color, yellow (orange in thicker sections) or blue (green in thicker sections). Haversian systems appear as “negative crosses” called Maltese or Brewster crosses. This means that fibers that run exactly parallel to the axis of the microscope are inactive in the polarized light; therefore, they show the same purple–red color as the background, whereas fibers that run only slightly obliquely already have a pale violet color. Fibers that run in polarized light parallel to the direction of the additive position are blue; those at right angles are yellow (Weber 1927). Moreover, examination of thin ground sections prepared from burnt or roasted bones in polarized light using a red first order (quartz) hilfsobject as a compensator is interesting. The effects of heat and fire lead to typical changes in the microstructure of the bony tissues (cf. Grimm and Strauch 1959; Schultz 1986; Piepenbrink and Herrmann 1988) that are also expressed in the bone collagen (Teschler-Nicola and Schultz 1984; Schultz 1986, 1997b). Furthermore, the intensity of the staining gives an accurate idea of the thickness of the thin ground section (e.g., in a thicker
section, i.e., approximately 75–95 µm, structures are orange and green; in a thinner section, i.e., approximately 50–70 µm, they are yellow and blue), which is an important help during preparation of the section.

It is surprising to many scientists that paleopathologists are still examining thin ground sections prepared from samples taken from archeological (i.e., macerated dry) bones because in histology and radiology various newer, more sophisticated, and more “modern” techniques are available. (The “modern” quality is very important to some researchers because they like to demonstrate that they are up to date and progressive. Thus, this species of scientists demonstrates an attitude that is not oriented to the real goal of research, which is represented by the effort to obtain the best results, but rather to their own personal, superficial reputations.) However, also Weber (1927:456) wrote “Die Untersuchung ungefärbter Schliffe zu diagnostischen Zwecken ist in der Pathologie der Knochenerkrankungen etwas Ungewöhnliches,” in which he demonstrated that the examination of thin ground sections was not frequent before World War II. Even so, the examination is regarded to be an antiquated technique, and some researchers try to make use of modern techniques such as digital radiology and multislice CT (an advanced form of helical computed tomography). Still, as already described (cf. Schultz 2001b), the quality of the results achieved by microscopic examination of thin ground sections is much higher than the results obtained by noninvasive techniques (Rühli et al. 2000, 2001). Therefore, the technique of choice is still microscopic investigation of thin ground sections. Only in cases such as the examination of archeological skeletons of native American Indians, where invasive examinations are not permitted, should researchers change to noninvasive techniques.

Microradiography detects the stage of ossification and the degree of calcification of bones and other tissues (e.g., Jowsey 1963, 1977). For many decades, this technique was used in paleopathology to diagnose diseases (e.g., Schultz 1986, 1988) and postmortem structural changes at the microlevel (e.g., Baud and Morgenthaler 1956) in subfossil and fossil bones. Microradiography produces reliable results, for example, the very fine lines found in the compact substance of long bones give the paleopathologist information similar to that from transverse linear enamel hypoplasias in the teeth and Harris’s lines in the metaphysis of long bones (Schultz 1986, 2001a; Herrmann et al. 1990). These lines actually represent cement lines, probably caused by arrested appositional growth. They should not be confused with the cement lines found, for instance, in secondary osteons. The lines are situated in the compact bone substance represented by secondary haversian bone oriented parallel to the external circumferential lamellae of the shaft of the long bone. Also, newly built formations on long bones, such as subperiosteal layers caused by mechanical stress, inflammatory processes, callus formations after bone fracture, and bone tumors (Figure 6-1a), can be identified and classified using this technique.

As mentioned, scanning-electron microscopy (SEM) is a helpful tool in paleopathology (e.g., Bell 1990). However, whereas using transmission light microscopy allows the observer to look through the bony tissue, using regular scanning-electron microscopy enables only the surfaces of bone to be inspected. Furthermore, the microstructure of archeological bone such as the lamellar formation of a bone trabecula is not really visible because it is, as a rule, very brittle and crumbles away at the cut or sawn face. However, if the backscattered electron mode (BSE mode) of a scanning-electron microscope is available for investigations, the internal structures of the bone tissue, for instance, the lamellae of a bone trabecula or the degree of mineralization of inorganic bone substance, can be studied in a similar way as in transmission light microscopy.

Using the high magnification capability of a SEM, even very fine details that represent intra vitam changes such as Howship’s lacunae and postmortem alterations such as plant roots and fungi become visible. These features can sometimes be important in differential diagnoses. For the diagnosis of perimortem cut marks and injuries, this technique also produces very good results (Wakely 1993).

There are a few other techniques, such as fluorescence microscopy (e.g., for the detection of the vestiges of postmortem or intra vitam fungi), phase-contrast microscopy, and interferential-contrast microscopy (e.g., examination of soil-living microorganisms), that are sometimes useful in paleopathology. However, these techniques are, as a rule, not routine and only rarely are needed.

Occasionally, close up endoscopy can contribute significantly to the microscopic research of dry bones. Magnifications up to approximately 50x are possible. With this technique, the internal surfaces of the endocranial face of the base and the vault of a skull, the paranasal sinuses, and the middle ear region, as well as the medullary cavity of long bones, can be viewed noninvasively by low power microscopy. This kind of examination is very helpful in establishing reliable differential diagnoses of inflammatory and hemorrhagic diseases of the skull.

### POSTMORTEM CHANGES

A corpse disintegrates in various ways. Autolysis is the breakdown of tissues by the action of enzymes contained in the tissues immediately after death. As a rule, the autolytic process does not change the microstructure of mineralized or calcified components of bone, but may destroy cells and soft tissues. It is important to know this if you are working on special problems at the molecular biological level. Further disintegration of soft tissues occurs through decomposition in which the tissues are separated or resolved.
into constituent parts or elements, mainly by bacteria, fungi, and arthropods. This process can take months or even years. Mineralized or calcified tissues are, as a rule, not affected. The term "diagenesis" characterizes the disintegration of mineralized or calcified tissues following decomposition.

Archeological bone is known to be affected under the earth by various, very similar factors as in decomposition (e.g., roots of plants, fungi, algae, bacteria, arthropods and their larvae, worms, protozoa, and mechanical agents such as water and crystals). The diagenesis process is characterized by the destruction of bones by physical and chemical agents produced by the foregoing factors, currently relatively little is known about the physiology of the fauna and flora of cadavers that are represented by the various organisms that have lived over many centuries on and in corpses, and cause decomposition and diagenesis (cf. Bass 1997; Hall 1997; Haskell et al. 1997; Rodriguez 1997). The damage produced by degradation can be diagnosed falsely by paleopathologists as lesions caused intra vitam by diseases (see the pseudopathology section). Many of the changes cannot be differentiated by macroscopic or radiological analysis, but are easily diagnosed by microscopic techniques (cf. Schultz 1986). For example, compact bone can be destroyed by characteristic tunnel-like canals caused by the postmortem growth of fungi or algae (Hackett 1981), and these tunnels can flow together (Figure 6-2) and produce relatively large destructive holes that macroscopically resemble intra vitam osteoporosis or vestiges of a metastasizing tumor. An apparently thickened newly built bone formation on the external surface of a bone that is macroscopically similar to the product of an inflammatory periosteal reaction (i.e., bone apposition) can be seen microscopically in a thin ground section to be a postmortem layer of aggregated crystals (e.g., brushite) that originated during diagenesis. Light or scanning-electron microscopic analysis of the netlike impressions on the internal lamina of the skull vault, macroscopically suspected to be vestiges of a hemorrhagic meningeal reaction, can show that they are the result of postmortem growth of plant roots. Snakelike, irregular grooves on the external skull (cf. Figure 6-42) vault co-occurring with a coarse bed can be caused by an inflammatory process of the scalp and the attached bone (e.g., nonspecific infection, treponemal diseases). However, in such a case, microscopic examination can exclude postmortem changes due to soil and water erosion.

It should be kept in mind that these postmortem factors often affect the results of immunohistochemical and molecular biological investigations (e.g., DNA and bone proteins) as well as the examination for trace elements and stable isotopes (Schultz 1986, 1997b; Schwartz and Schultz 1994). Therefore, microscopic investigation is indispensable prior to examination of archeological remains by chemical and physical techniques.

Sometimes, bones in the ground are preserved by protective surroundings. Then, the process of diagenesis works very slowly and incompletely or even is suspended. This causes, for instance, development of fossilization. In such cases, the bone is frequently preserved for many thousands of years in a cave or in a rock shelter. However, subfossils such as prehistoric bones also have a good chance of being unaffected by diagenesis if elements such as copper (Cu), manganese (Mn), and even iron (Fe) are sufficiently concentrated in the burial environment. Microscopic investigation in combination with element analysis makes a demonstration of the causes and processes of preservation feasible. It is well known that Cu ions preserve organic materials very well, because they are bactericidal (Schultz 1997b). The surfaces of archeological bones found close to bronze jewelry or bronze weapons are stained greenish or even green during the hundreds or thousands of years of contact. In most cases, the histological analysis of these greenish stained bone samples reveals very well-preserved bone substance that can even be in almost the same state as fresh bone. The Göttingen research group, consisting of S. Berg, W. Bonte, H. Kijewski, and M. Schultz, studied bone samples collected from different prehistoric and early historic sites in Europe, the Near East, and North America by morphological and physical techniques. The results are very interesting (cf. Schultz 2001b). Manganese preserves bone almost as well as copper, and even iron protects bone structures to a certain degree. The stage of morphological preservation of bone substance actually correlates with the concentration of soil minerals that have invaded the bone (Schultz 2001b).

Destruction in archeological bones is often caused by the mechanical influence of the soil in which the corpse was

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**FIGURE 6-2** Various factors of diagenesis. A cross section through a long bone fragment of an adult individual from Klinzing (southern Germany), Late Roman Period. The compact bone substance is represented by haversian systems: a = haversian canal. Severe destruction mainly was caused by fungi. This undecalcified thin ground section (25 μm) was stained with fuchsine and was viewed through the microscope in plane light. Magnification 100x.
buried. Water and sand can change bone surfaces (Figure 6-3) or even the internal structures of bone in a relatively characteristic manner (Wittwer-Backofen et al. 2001).

The microscopic examination of skeletal remains can even prove where a burial was primarily placed. As a rule, small particles of the soil in which the burial was primarily laid, can be detected by the microscope in the spaces of cancellous bone. With polarized light, microscopic analysis can reconstruct the quality and the composition of the soil (e.g., sand, loess, or humus). Thus, there is evidence of a probable secondary burial if the soil particles from the interior of the bone are different from the soil particles from the burial pit.

Plant roots are one of the most common causes of post-mortem bone destruction (Figure 6-4). Large roots create distinctive traces on bone surfaces that are, usually, not difficult to diagnose (Schultz 1997b). However, very small, hairlike roots produce fine defects that can be mistaken for the vestiges of diseases, for instance, a sulcus representing a blood vessel impression on the internal lamina of the skull vault or an intra vitam cut mark (Schultz 1986, 1997b). It is important to know that these fine roots can also grow into the paranasal sinuses and the medullary cavities and produce pseudopathology.

The large group of organisms that destroy archeological skeletal remains include fungi, algae, and bacteria (Schultz 1986, 1994a, 1997b). Particularly fungi (Figures 6-5 and 6-6) and algae create small holes, cavities, and channellike structures (Figure 6-2). The latter are called bohrkanäle (Wedl 1864) or tunnels (Hackett 1981). Such changes are found in the majority of archeological bones and can be observed in plane light. Using fluorescence microscopy or phase-contrast microscopy and scanning-electron microscopy, the effect of these organisms on skeletal tissue can be studied (e.g., Basset et al. 1980; Keith and Armelagos 1982, 1988, 1991; Piepenbrink 1984; Schultz 1986, 1997b).

Sometimes we see growth traces of very small bacteria that grow like mycelia.

Microscopically, remains of arthropods are frequently seen in bones or mummified tissues recovered in archeological excavations (Figures 6-7 and 6-8). In many cases, the origin of these small intruders is uncertain, because of the poor preservation of the findings. Therefore, particularly in the case of insect remains, it is difficult to decide whether these specimens parasitized the body during its lifetime, appeared immediately after death in the cadaver, or used

![Figure 6-4](image-url)  **Figure 6-4** Various factors of diagenesis. The fragment of long bone from preclassic Tetelpan (central Mexico) shows a cross section through a very small root in a large blood vessel canal. The undecalcified thin ground section (50 µm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 160x.

![Figure 6-5](image-url)  **Figure 6-5** Various factors of diagenesis. Fungus (probably *Aspergillus flavus*) in the haversian canal of compact bone substance of the left tibia (E-4; Klosterneuburg, Lower Austria, Early Modern Times). The undecalcified thin ground section (50 µm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 160x.
the macerated bones during their time under ground as a habitation (Schultz 1986, 1997b). For differential diagnoses, identification of the remains of insects and their larvae, worms, protozoa, spores of fungi and bacteria is necessary. Occasionally, parasites that affect the living resemble specimens that live in the cadaver or belong to the fauna and flora of the earth. Only reliable diagnoses established by microscopic research make the study of infectious diseases of past populations feasible. Thus, exact knowledge of these faunal and floral specimens is an important dimension of our knowledge of human disease in the past.

Under certain conditions of diagenesis, new crystals (cf. Figures 6-9 and 6-10) can develop within the bone that originate from natural bone apatite (e.g., brushite, which is acidic calcium phosphate; Herrmann and Newesely 1982). These newly crystallized structures can aggregate and almost completely break up interior structures of a bone, similar to the way that frozen water can burst a full, stoppered bottle (Schultz 1986, 1997b, 2001b).

**GENERAL COMMENTS ON PROLIFERATIVE REACTIONS**

Ancient bones caries, fractures, genetically caused malformations of bones, osteoarthritus, myositis ossificans, various
Diseases that can be diagnosed by microscopy are, as a rule, classified according to specific features. Numerous books and articles that deal with pathological bone changes in recent pathology are available to help diagnose ancient bones (e.g., Jaffe 1972; Schajowicz 1981; Resnick and Niwayama 1981; Revell 1986; Adler 1998). However, we have to remember that in paleohistopathology of dry bones, the diagnostic criteria are often quite different from those used in recent pathology where soft tissues and cells are available as important diagnostic markers. The classification of diseases investigated by paleohistopathologists therefore does not necessarily always conform to that used by clinical pathologists. In paleohistopathology, morphological features must first be classified prior to establishing a final diagnosis.

FIGURE 6-9 Crystals in ancient bones. Transverse section through a bone fragment of Australopithecus from Swartkrans. Spongiosa are filled with crystals caused by the fossilization process. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hill object as a compensator. Magnification 25x.

FIGURE 6-10 Crystals in ancient bones. Cross section through a compact bone fragment from preclassic Tetelpan (central Mexico). In the small blood vessel canal, crystals built up during diagenesis. Scanning-electron microscopic image. Magnification: bar = 2 μm.

inflammatory bone processes, such as nonspecific osteomyelitis and periostitis, and many osteoblastic and osteoclastic bone tumors, frequently can be macroscopically diagnosed. Moreover, certain deficiency diseases, for example, scurvy, rickets, and anemia, often produce characteristic changes in bone tissue that can also be observed macroscopically. However, reliable diagnoses are not always easy to establish. Luckily, many of these diseases cause specific changes not only at the macroscopic, but also at the microscopic level, and the results of a microscopic investigation can provide reliable differential diagnoses that, in many cases, are quite specific.

An interesting observation is that in the paleopathological literature (e.g., Tyson 1997) contributions that deal with the histology of bone lesions or microscopic research on archeological skeletal remains are relatively scarce. Even authors or editors of comprehensive books, such as Jarcho (1966), Brothwell and Sandison (1967), Steinbock (1976), Živanović (1982), Ortner and Putschar (1985), Ortner and Auferheide (1991), Dastugue and Gervais (1992), and Auferheide and Rodríguez-Martin (1998), have not really presented any light microscopic research on ancient bone. This is then the reason why, in this chapter, emphasis is laid on reliable microscopic diagnosis of diseases using thin ground sections prepared from dry bone tissue.

As already mentioned, the main challenge in microscopic investigation of archeological skeletal remains is the absence of soft tissues and cells, which play an important role in pathological investigations on recent materials. Therefore, a cytological investigation cannot be carried out and a true histological examination of archeological skeletal remains in the primary sense of the term “histology” (where histology means the study of tissues) is hardly possible. However, the mineralized components and some organic features, such as bone collagen, can still be studied by histology. In the diagnosis of pathological changes in ancient skeletons at the microlevel, a very important role is played by the architecture of the cortical, compact, and spongy bone structures, and particularly by the architecture (Figure 6-63) of the newly built bone formations (Schultz 1986, 1993a, b). There is a current opinion that bone tissue always acts in the same way when affected by inflammatory diseases. At the macroscopic level, different diseases can indeed some-
General Comments on Proliferative Reactions

An inflammatory process that affects the periosteum, for instance, hematogenous osteomyelitis or treponemal diseases, produces changes that may not be differentiated by macroscopic investigation. However, by microscopic analysis, a pattern of features represented by the architectural elements of the cortical, compact, and spongy bone substances that are associated with a particular disease can almost always be distinguished. It can even be said that such a pattern is not found in the exact same constellation in any other disease. The classification and interpretation of these morphological features found in newly built bone formations of florid and slowly developing chronic processes make diagnoses more reliable and the pattern of the changes provides an efficient key to a diagnosis. The problems involved in differential diagnosis emphasize the need to consider the total distribution pattern of abnormal lesions in the skeleton, rather than each one separately. There are specific morphological features at the microlevel such as faserfilz osteons (cf. Figure 6-59) described by Knese et al. (1954) in nonpathologically changed adult bones. However, this kind of osteon is also found frequently in slowly growing primary osteoblastic bone tumors (Schultz 1978, 1986). Furthermore, there are polsters and grenzstreifen (in treponemal diseases; cf. Figures 6-18 and 6-19), which are usually irrelevant for recent pathology, but enable the paleopathologist to make relatively reliable diagnoses. Also the number and distribution of Howship's lacunae give a relevant impression of the nature of an osteoclastic or osteolytic process (Figure 6-12; see also Figures 6-41c and 6-48b). At the end of the 19th and in the first half of the 20th century, bone pathologists often diagnosed macerated bone with similar methods and techniques to those used by modern paleopathologists (e.g., Beitzke 1934a; Konschegg 1934; Gruber 1938; Lauche 1939). In almost all cases, the group of diseases characterized by various bone reactions (e.g., proliferative or osteolytic) or at least the nature of the disease can be determined (e.g., inflammatory or hemorrhagic), although occasionally an exact diagnosis is difficult. Thus, the paleohistopathologist must become very familiar not only with the microarchitecture, but also with the pathophysiology of bone.

FIGURE 6-11 Dorsal view of the right ischial tuberosity of a 40–49-year-old male from Pergamon (western Anatolia), Late Byzantine Period, showing irregular porotic newly built bone formation (arrows). See also Figure 6-63.

FIGURE 6-12 Archeological evidence of cancer. Surface of the occipitolateral wall of the left maxillary sinus of a 35–45-year-old male from Sayala (Egyptian Nubia), Ind. I-3, Coptic Period. Vestiges of primary osteoclastic tumor represented by Howship's lacunae (arrows) are covered by mummified remains of soft tissue = a. The undecalcified thin ground section (50 µm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 100x.
However, these two kinds of processes frequently occur together and this makes diagnoses difficult. Thus, at least a basic medical knowledge is required if histopathological work is to be successful.

In many diseases, similar mechanisms of bone behavior can be observed. Thus, we frequently find the same basic reactions of bone behavior in various diseases that produce a characteristic morphological pattern of bone architecture. This morphological pattern persistently influences the gross morphology of a bone and this is what the paleopathologist first observes in a pathologically affected bone. Therefore, particularly for paleopathologists who normally are not

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<th>TABLE 6-1 Proliferative Reactions: A Classification of Characteristic Morphological Patterns, with Relevant References</th>
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I. Proliferative reactions (characterized by the addition of new bone to external and endocranial surfaces)

A. External periosteal reactions (e.g., long bones and skull vault)

1. Hemorrhagic, that is, in subperiosteal hematoma (e.g., caused by trauma; see Schultz 1987a); scurvy (e.g., Schultz 1986, 1987a; Schultz and Teschler-Nicola 1987b, d). In contrast to inflammatory processes, changes due to hemorrhagic processes are only found that are external to the original bone surface. The original bone substance is not affected by the pathological process. Changes are expressed by:
   a. Small hemorrhage or peripheral region of large hemorrhage; a thin layer in the form of a slippetlike cover of newly built bone.
   b. Center of large hemorrhage: Relatively short, bulky bone trabeculae showing extensive bridging. Rarely, in recidivation, several layers can be developed.

2. Inflammatory, that is, in nonspecific and specific periostitis (e.g., caused by nonspecific osteitis or hematogenous osteomyelitis, treponemal osteitis, or osteomyelitis; see Schultz 1986, 1987a; Schultz and Teschler-Nicola 1987b, d). In contrast to hemorrhagic processes, inflammatory processes always affect the bone surface and the outer layer and frequently also the deeper structures of the original bone substance. Changes are expressed by:
   a. Small area or extremely peripheral region of large area affected; thin layer in the form of a slippetlike cover of newly built bone.
   b. Middle-sized or large area affected; relatively long and thin bone trabeculae that are mainly oriented slightly irregular in parallel order. There is only slight bridging. Relatively frequently, several layers can be developed (recidivation). In this case, there is an extensive bridging, in particular just at the level of an episode.

3. Tumorous, that is, as periostosis (e.g., caused by primary or secondary bone tumors; see Schultz 1986, 1993c). Tumorous processes may affect the bone surface; in advanced stages also the deeper structures of the original bone substance. Changes are expressed by structures very similar to the inflammatory changes described before. However, as a rule, the trabeculae show a more regular development.

4. Circulatory, that is, as periostosis (e.g., caused by hypertrophic pulmonary osteoarthropathy or Bamberger–Marie disease; see Schultz 1987a; Teschler-Nicola and Schultz 1984). There are relatively thick secondary layers at original bone surfaces. Sometimes, short and bulky trabeculae are developed that are similar to changes observed in hemorrhagic processes. Vestiges of recidivation in the form of stratified formations are frequently seen.

B. Endocranial meningeal reactions (skull vault and base)

1. Hemorrhagic, that is, in epidural hematoma (e.g., caused by trauma, scurvy, and pachymeningosis haemorrhagica interna; see Carli-Thiele 1996; Kreutz 1997; Schultz 1987a, b, 1990, 1993a). In contrast to inflammatory processes, changes due to hemorrhagic processes are only found external to the original bone surface. The original bone substance of the internal laminae can be affected by pressure atrophy due to the pathological process. Changes are expressed by:
   a. Beginning stage of organization (remodeling): small, patchlike areas of narrow, branching blood vessel impressions.
   b. Slightly advanced stage of organization (remodeling): porotic plates that can become relatively thick (large hematoma), covering the blood vessel impressions mentioned before.
   c. More advanced stage of organization (remodeling): groups of tonguelike smooth plates that are separated by an extensive netlike aggregation of small blood vessel impressions.

   These lesions are mainly situated in the digital impressions but can also spread over larger areas of the skull vault.

2. Inflammatory, that is, in nonspecific (bacterial) and specific (tuberculous) meningitis, meningoencephalitis, and pachymeningitis. In contrast to hemorrhagic processes, inflammatory processes always affect the bone surface, frequently also the deeper structures of the original bone substance (particularly in tuberculous meningitis).

   a. Relatively fresh (i.e., florid) process:
      i. In nonspecific (bacterial) and specific (tuberculous) meningitis changes are expressed by smooth and flat platelike newly built bone formations that are, as a rule, oriented tangentially to the endocranial surface. There are isolated plates that can also be confluent as one layer. Several layers are possible (recidivation). These lesions are frequently found in digital impressions but also spread over larger areas in an advanced stage (see Carli-Thiele 1996; Kreutz 1997; Schultz 1990, 1993a, b; Schultz and Kunter 1999).
      ii. In specific (tuberculous) meningitis changes are expressed as described before. However, additionally, particularly at the skull base and the basal regions of the vault, there are small impressions that can be isolated or grouped together (see Jankauskas and Schultz 1999; Kreutz 1997; Schultz 1999a; Tempel 1993; Tempel and Schultz 1994).

   b. Non-specific and specific lesions: in more advanced organization stages, the contours become indistinct and the platelike character will be lost by the remodeling process. In specific lesions only, the small impressions become organized, that is they start to be filled by newly built bone formations (remodeling: see Schultz 1999a; Tempel 1993).

3. Tumorous, (e.g., in meningoeoma). Tumorous processes may affect the bone surface and, in advanced stages, also the deeper structures of the original bone substance. Changes are expressed by irregular bulging of relatively dense newly built bone formations; no typical trabecular growth.

* Diagnoses using light microscopy and thin ground sections prepared from archeological specimens (see Schultz 2001b).
practicing bone pathologists but rather anthropologists, a special categorization is recommended (cf. Table 6-1) based on characteristic morphological patterns. This categorization is based on macroscopic investigation and allows a step by step diagnosis using the characteristic microscopic morphological features to determine a final diagnosis. This categorization does not make use of the traditional pathological criteria of recent pathology; however, in combination with the results of the macroscopic and radiological investigation, the diagnosis is highly reliable.

As an example of one of the most important basic reactions, proliferative changes are described and discussed (see Table 6-1). Characteristic for bone behavior, proliferative changes are observed in some metabolic diseases (Figures 6-13 and 6-14), in infectious bone diseases (Figures 6-15 to 6-19; see also Figures 6-30, 6-31, 6-36 to 6-50, 6-60 to 6-62), sometimes in circulatory disorders (Figure 6-20), in bone tumors and tumorlike conditions (Figures 6-1, 6-12 and 6-21 to 6-24), and in miscellaneous other

**FIGURE 6-13** Porotic hyperostosis in a subadult skull vault. (a) Line drawing based on original undecalcified ground sections of the left parietal bone of a recent child (age group Infans II, 7-14 years). There is complete transformation of original structures to the characteristic gracile trabeculae due to rickets with reduction of the modules of the red bone marrow (diploë). The external vault surface is covered by the typical rachitic osteophyte (i.e., osteoplaque). Magnification approximately 1x. (b) Microscopic features of a frontal section through the left parietal bone in this case. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. The trabeculae of the diploë are gracile and the modules of the red bone marrow are reduced = a. Well pronounced rachitic osteophyte = b, (i.e., osteoplaque). From the historic collection of the Department of Pathology of the University of Göttingen (case GP-1985903). Magnification 25x.

**FIGURE 6-14** Porotic hyperostosis in the subadult skull vault. (a) Line drawing based on original undecalcified ground sections of a fragment of the parietal bone of a newborn to 3-month-old infant from Ikiztepe (northern Anatolia), burial 53, Early Bronze Age. The skull bone is completely changed due to rickets. The external lamina is built up of squamous plates that represent the rachitic osteophyte (i.e., osteoplaque). The trabeculae of the diploë are completely irregular and gracile, the modules of the red bone marrow are reduced, and the internal lamina is partly splintered. Magnification approximately 2x. (b) Microscopic features of a sagittal section through a fragment of the right frontal bone. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. The trabeculae of the diploë are gracile and the modules of the red bone marrow are reduced = a. The external surface of the vault is built up by flat, atrophic trabeculae that represent the fresh rachitic osteophyte = b (i.e., osteoplaque). Magnification 25x.

**FIGURE 6-15** Vestiges of nonspecific periosteal reactions in the postcranial skeleton (cf. Schultz 2001b) shown in a cross section through a rib of a 35-49-year-old male from Boğazkale (central Anatolia), burial 61B/85, Early Byzantine Period. Vestiges of pleurisy; a = original cortex of the rib; b = fissural gap between external bone surface and c = newly built bone formation. Noxa affected periosteum from the pleura. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.
Vestiges of nonspecific periosteal reactions in the postcranial skeleton (cf. Schultz 2001b) shown in a cross section through the tibia of a 2-4 (12) year-old child from Bettingen (Switzerland), Ind. 2/K-2, Late Middle Ages. Vestiges of acute periostitis: a = original compact bone of the shaft; b = newly built bone formation. Up to the time of death no pathological changes in the compact bone substance occurred. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.

Vestiges of nonspecific periosteal reactions in the shafts of long bones caused by venereal syphilis shown in a cross section through the right femur of an adult individual (D-9) from Klosterneuburg (Lower Austria), Early Modern times. Vestiges of venereal syphilis in the form of pronounced polsters: a = primary (older) newly built formation of pathologically changed bone; b = polster; c = narrow grenzstreifen. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.

Vestiges of nonspecific periosteal reactions in the postcranial skeleton (cf. Schultz 2001b) shown in a cross section through the right fibula of a 35-49-year-old male from Boğazkale (central Anatolia), burial 37/83, Early Byzantine Period. Vestiges of chronic, relapsing periostitis (at least three wavelike processes) due to osteomyelitis: a = original compact bone of the shaft; 1, 2, and 3, vestiges of relapsing periostitis. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.

Vestiges of periosteal reactions in the shafts of long bones caused by venereal syphilis shown in a cross section through the left tibia of an adult individual (E-4) from Klosterneuburg (Lower Austria), Early Modern times. Vestiges of venereal syphilis in the form of small polsters: a = primary (older) newly built formation of pathologically changed bone; b = polster. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light. Magnification 25x.

Vestiges of nonspecific periosteal reactions in the postcranial skeleton (cf. Schultz 2001b) shown in a cross section through the right fibula of a 35-49-year-old male from Boğazkale (central Anatolia), burial 37/83, Early Byzantine Period. Vestiges of chronic, relapsing periostitis (at least three wavelike processes) due to osteomyelitis: a = original compact bone of the shaft; 1, 2, and 3, vestiges of relapsing periostitis. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.

Conditions (Figures 6-25 and 6-26) as well as in healing of bone after fracture (Figure 6-27a-d). Proliferative changes are found in all parts of the skeleton, not only in long bones and the skull. Other basic reactions of bone behavior include osteoclastic changes observed in various groups of diseases (e.g., inflammatory and tumorous diseases). Furthermore, porotic changes in the skull vault and the orbital roof are frequently associated with a marked thickening of the affected bone structure and represent a morphological syndrome (see Table 6-2). To clarify how microscopic diagnosis usually works in paleopathology, examples from some of the categories presented in Tables 6-1 and 6-2 are discussed subsequently. Finally, a few groups of morphological patterns (cf. Tables 6-1 and 6-2) as well as cases of various diseases
FIGURE 6-21 Archeological evidence of cancer. Invasive growth of irregular bone trabeculae (metastasis) and secondary osteoblastic reaction filling osteoclastic defects in the sacrum of a 25–55-year-old male from Truchtliefingen (southern Germany), burial 10, Early Middle Ages, Alamannic. Scanning-electron microscopic image. Magnification: bar = 400 μm.

are presented that describe the most important morphological features of macerated tissue at the microlevel.

Proliferative (productive) reactions in bony tissue can be observed best on the external and internal surfaces of bones. Thus, in this chapter, examples of these reactions are presented from two different topographic areas of the human skeleton: the periosteal (i.e., the external surface of the shaft of long bones) and the meningeal (i.e., the endocranial surface of the skull). There are obviously also various regions of the skeleton where proliferative processes of the periosteum can be observed, such as at the internal surfaces of ribs (Figures 6-28 and 6-15) where pleurisy and empyema of the costal pleura affect the periosteum. These changes are not always a symptom of or characteristic of tuberculosis of the lungs, although such changes can accompany a tuberculous process (Pfeiffer 1991; Wakely et al. 1991).

PERIOSTEAL REACTIONS ON LONG BONES

Bones frequently have a coarse surface at muscle attachments. Sometimes, however, newly built formations can be observed in these areas from bone apposition (Figure 6-11). Without microscopic analysis, the nature of such a lesion cannot be determined reliably. Relatively frequently, the cause of the origin of such new bone structures is excessive
6-26 Porotic hyperostosis in the human skull shown in a sagittal section through the left frontal bone of a mature individual with osteitis deformans (Paget's disease; same case as Figure 6-25). The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hillssobject as a compensator. The short irregular bone trabeculae characteristic of this disease present a partly mosaic structure. Collection of the Institute of Legal Medicine of the University of Vienna (case RMW-Schl). Magnification 25x.

6-25 Porotic hyperostosis in the skull vault. Line drawings based on the original undecalcified ground sagittal section through the left frontal bone of a mature individual. Excessive enlargement of the skull vault is due to osteitis deformans (Paget's disease). External and internal lamina as well as the regular diploë are completely transformed to short irregular bone trabeculae characteristic of this disease. Only the space of a diploic vena (oval hole) and some other irregular holes, which perhaps represent some very few residuals of the original modules of the red bone marrow, are still in place. Collection of the Institute of Legal Medicine of the University of Vienna (case RMW-Schl). Magnification approximately 1x.
mation that is found, for instance, on the external surface of
the bone shaft. The external basic lamella remains intact
and there are no evident changes in the compact bone sub-
stance (Figures 6-29 and 6-64). The short bony trabeculae
of this subperiosteal formation are relatively coarse and
bulky, often forming short-bridged structures (Figure 6-29,
cf. Figure 6-28).

It is well known that scurvy, particularly in subadults, is
accompanied by widespread subperiosteal bleeding that
frequently occurs after slight trauma or even without trauma.
The vestiges of such a hematoma can also be diagnosed in
archeological skeletal remains because of the characteristic
newly built bone formations. In dry bones, the main
features caused by chronic scurvy are subperiosteal new
bone formations from mineralized hemorrhagic processes.
Such alterations are frequently found on the shaft of the
long bones, on the ectocranial and also sometimes on the
endocranial surface of the skull vault, and in the jaw area.

In subadults, these pathological changes are usually more
pronounced, because in this age group bone metabolism is
more active.

Periostitis creates characteristic changes that can be
grouped into different morphological pictures. In a florid
inflammatory process of the periosteum, the bone trabeculae
take on a different shape from those in a hemorrhagic
process. The relatively thin, often parallel trabeculae are
oriented radially to the bone surface (Figure 6-16). The
age-dependent basic lamellae are still in place and the
neighboring compact bone substance mostly is affected by
the inflammatory process. Only at the beginning of an
inflammatory process, and then if it is caused by an external
noxa, might the basic lamellae and the compact bone sub-
stance be free of pathological changes (Figure 6-16). In
chronic periostitis, the periosteal reaction is only one of
several pathomorphological symptoms. In this stage of
disease, we find not only periostitis, but also osteitis (i.e.,

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TABLE 6-2 The Phenomenon of Porotic Hyperostosis: The Pathological Processes that Can
Contribute to a Morphological Syndrome

| I. Porotic hyperostosis (characterized by a thickened bone structure and a porotic surface) |
|---|---|
| A. Skull vault | |
| 1. Inflammatory processes | |
| a. Inflammatory processes of the scalp. | |
| b. Periostitis of the external skull vault. | |
| c. Nonspecific and sometimes also specific osteitis and osteomyelitis of the skull vault. | |
| The characteristic changes of porotic hyperostosis can occur after healing. As a rule, the thickening of the skull vault and the porosity are not very well pronounced. | |
| 2. Hemorrhagic processes | |
| a) Subperiosteal hematoma caused by trauma (e.g., birth); relatively frequently seen in infants and children. In infants, the changes can be relatively well developed. | |
| b) Subperiosteal hematoma caused by scurvy (see 4b); frequently seen in infants and children. The changes can be very well pronounced and sometimes reach an enormous size. Macroscopically, the changes are very similar to the changes found in cavernous hemangioma and anemia. | |
| 3. Tumors and tumorous processes | |
| a. Cavernous hemangioma. This is a rare tumor. Macroscopically, the changes are very similar to the changes found in hemorrhagic (hematoma) and anemic processes. | |
| b. Meningioma. Not a very rare tumor, however, newly built bone formations at the external skull surfaces that represent porotic hyperostosis are very rare. Macroscopically, the changes are very similar to the changes found in hemorrhagic (hematoma) and anemic processes. | |
| 4. Dietary disorders | |
| a. Various kinds of anemia (see 5), such as nutritionally caused iron-deficiency anemia. The well known changes ranges from slight to extremely severe. Macroscopically, the changes are very similar to the changes found in hemorrhagic processes (hematoma) and cavernous hemangioma. | |
| b. Scurvy (see 2b); frequently seen in infants and children. The changes due to hemorrhagic processes can be very well pronounced and sometimes reach an enormous size. Macroscopically, the changes are very similar to the changes found in anemia and cavernous hemangioma. | |
| c. Rickets; relatively rarely seen (depends on the geographical region and the nutritional situation). As a rule, the changes are very discrete, which means that a very fine porosity can be well pronounced; however, the thickening is only slightly developed. | |
| 5. Genetic causes | |
| a. For example, some kinds of anemia (see 4a), such as sickle-cell anemia and thalassemia. The changes ranges from slight to extremely severe. Macroscopically, the changes are very similar to the changes found in hemorrhagic processes (hematoma) and cavernous hemangioma. | |
| 6. Other causes | |
| a. For example, other kinds of anemia that are not due to nutritional stress, that is, anemia caused by parasites (e.g., worms, and plasmodia)... | |
| b. Meningioma. Not a very rare tumor, however, newly built bone formations at the external skull surfaces that represent porotic hyperostosis are very rare. Macroscopically, the changes are very similar to the changes found in hemorrhagic (hematoma) and anemic processes. | |
| a) Subperiosteal hematoma caused by trauma (e.g., birth); relatively frequently seen in infants and children. In infants, the changes can be relatively well developed. | |
| b) Subperiosteal hematoma caused by scurvy (see 4b); frequently seen in infants and children. The changes can be very well pronounced and sometimes reach an enormous size. Macroscopically, the changes are very similar to the changes found in cavernous hemangioma and anemia. | |
FIGURE 6-27 Bone changes subsequent to fracture of the skull in an adult individual. (a) Line drawing of the right parietal, true to the original undecalcified ground sections (25 μm) that demonstrates features of skull fracture. Fracture of skull vault: a = fracture callus; b = product of meningeal reaction. Magnification approximately 1×. (b) Line drawing of the frontal bone, true to original undecalcified ground sections (25 μm), that demonstrates features of skull fracture. Plate-like structure originally covered the pathological process (e.g., hemorrhage cf. 6-66). For detail, see Figure 6-66. Magnification approximately 1×. (c) Undecalcified thin ground sections (50 μm) viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. The fracture site in the right parietal bone: a = fracture callus; b = internal lamina of external fragment; c = external lamina of internal fragment; d = region of bone resorption (i.e., surface of fracture) between the callus = a and the original vault bone = c. Magnification 25×. (d) Undecalcified thin ground sections (50 μm) viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. a = internal lamina; b = diploe; c = product of meningeal reaction. Area of feature b in Figure 6-27a. Magnification 25×. Historic collection of the Department of Pathology of the University of Göttingen (case GP-198581).

FIGURE 6-28 Porotic layers on the internal rib surface in a 4–5-year-old child from İkiztepe (northern Turkey), burial 88, Early Bronze Age. (a) Macroscopic view. (b) Newly built bone formation (arrow) probably caused by a hemorrhagic process. Parts of the short-bridged structures that characterize such a process are lost by postmortem destruction. The undecalcified thin ground section (50 μm) was viewed through the microscope in plane light. Magnification 25×.
Periosteal Reactions on Long Bones

Reporting on treponemal diseases, Hackett (1976) described the different stages of typical syphilitic bone changes in the skull and long bones very exactly. Unfortunately, bone lesions caused by syphilis are frequently very similar to alterations caused by nonspecific bone diseases, particularly in long bones. By using polarized light in light microscopy, the internal bone structure, especially the arrangement of the collagenous fibers, can be seen and structures typically built up by different disease processes become visible. Thus, the results of the microscopic investigation, in combination with the results of the macroscopic, radiological, and scanning-electron microscopic research, provide a reliable diagnosis. As previously mentioned, there are telltale signs at the microlevel, such as (1) polsters and (2) grenzstreifen, that are characteristic of treponemal diseases. These are now considered in more detail.

Polsters

Polsters are characteristic features at the microscopic level (Figures 6-18 and 6-19) and are often found in chronic treponemal diseases of the long bones (Weber 1927; Michaelis 1930; Schultz and Teschler-Nicola 1987b; Schultz 1994b). They consist of parallel lamellae that at the periosteal level are arranged in the form of pillow-like newly built bone formations demarcated by periosteal blood vessels that develop during the course of the inflammatory process (hypervascularization). The growth of this pathologic bone formation, which is a superficial layer, progresses relatively slowly and the polsters show a regular and relatively homogeneous structure. In contrast, in hematogenous osteomyelitis, the periosteal newly built bone formation is irregular and shows various structures that are the result of the relatively rapid growth associated with a relatively high remodeling rate. Particularly well developed polsters are a good indicator of treponemal diseases (Schultz 1994b). However, in lepromatous periostitis, polsterlike structures that are rudimentarily developed and relatively flat (Figures 6-30 and 6-31) also can be observed (Blondiaux et al. 1994; Schultz and Roberts 2002 in press).

Grenzstreifen

Generally, a grenzstreifen or grenzlinie (Figure 6-19) can be observed in chronic treponemal diseases (Schultz and Teschler-Nicola 1987b; Schultz 1994b) and is never found in hematogenous osteomyelitis of long bones (Weber 1927; Schultz and Teschler-Nicola 1987b; Schultz 1994b). At first sight, the grenzstreifen and older unremodeled bone material embedded in a nonspecific inflammatory process look the same. However, the grenzstreifen is, as a rule, a very fine line or a narrow, ribbon-like structure that is the original external surface of the bone shaft (remains of external circumferential lamellae) and newly built lamellae.
that originated during the first infection of the peristeum due to the pathological process, i.e., *Periostitis syphilitica* (Weber 1927). Thus, the grenzstreifen is always caused by the relatively slow transmigration of a specific inflammatory process in the primary periosteal region. On the outside of the grenzstreifen, the newly built bone formation is present as a solid mass. However, in nonspecific inflammatory bone disease, for example, in hematogenous osteomyelitis, the process is very aggressive and grows rapidly, causing extensive destruction. The bone is rapidly eaten away and new bone formation also builds up rapidly. Therefore, large pieces of the old bone shaft might still be in place, but are embedded in the newly built bone formation. This structure is not a grenzstreifen. Grenzstreifen can, therefore, be a useful indicator with which to diagnose chronic treponematoses by microscopy. In chronic leprosy, no characteristic grenzstreifen (Figure 6-31) can be observed (Schultz and Roberts 2002, in press). In contrast, in treponemal diseases, including endemic syphilis, not only do alterations take place in the subperiosteal bone, but additionally osteoclastic changes occur in the endostial bone and the bony trabeculae of the medullary cavity as well as in the compact bone substance of the shafts of the long bones affected (Schultz and Teschler-Nicola 1987b; Schultz 1994b; Kuhnen et al. 1999; Schultz and Roberts 2002, in press). Thus, the osteolytic changes in the shafts of long bones correspond to the findings already by Hackett (1976) and the microscopist will not only see resorption holes and corroded structures, such as incomplete trabeculae, but also vestiges of an extensive remodeling process. The latter is usually not found to this extent in hematogenous osteomyelitis.

The last group of periosteal newly built bone formations are observed in tumorous diseases, in the healing process of bones after fracturing, and in processes of the deep veins as well as primary and secondary hypertrophic (pulmonary) osteoarthropathy (cf. Figure 6-20). In these processes the resulting structures are not produced by an inflammatory process; therefore, the term *periostitis* is, strictly speaking, incorrect and the term *periostosis* should be used instead because in Latin terminology, the suffix "-osis" characterizes a noninflammatory process and the suffix "-itis" denotes an inflammatory process.

In general, a spindle-shaped enlargement of the bone shaft is characteristic of various periosteal reactions, such as periostosis in bone tumors, but also as periostitis in treponemal diseases (e.g., *Periostitis syphilitica*). However, at the beginning of a tumorous periosteal reaction, the lesions are usually flat layers. The compact bone substance is not affected at this stage. At an advanced stage, the external area of the newly built bone formation is frequently constructed of spicula and the compact bone substance can be severely affected by sclerotic or osteoclastic changes. As a rule, a tumor periostosis looks different (cf. Figure 6-24) from the product of an inflammatory process (periostitis; cf. Figures 6-16 and 6-17).

The newly built bone induced by the periosteum during the healing process following a fracture is called callus. This kind of periosteal bone takes on various shapes, because muscles can insert (area of Sharpey's fibers) close to the fracture line and the affected periosteum influences its development. Similar conditions regarding the initiation and
the macroscopic morphology of new periosteal bone formations are observed in processes of the deep veins as well as in primary and secondary hypertrophic osteoarthropathy. However, as a rule, in these cases the new periosteal bone is relatively moderately developed.

**MENINGEAL REACTIONS**

On the endocranial lamina of the skulls of subadults, vestiges of meningeal reactions are often found (Schultz 1987a, b, 1990, 1993a, b, 2001a; Schultz and Teschler-Nicola 1987a; Templin 1993; Carli-Thiele 1996; Kreutz 1997). Koganei (1911) reported that, based on dissection work, the German pathologist Virchow established diagnoses of acute cases of an inflammation of the skull bones that were accompanied by the reaction of the meninges. These diagnoses came very close to the understanding of pathological conditions we have today. In the course of dissection, Koganei (1911) also observed newly built layers that he characterized as rich in Sharpey’s fibers. He described the macroscopic morphology of these changes as follows: “… eigentümlich mattes, weissliches, reifähnliches Aussehen” (Koganei 1911:123). Furthermore, he characterized the newly built formation in their microscopic morphology as follows: “… (sind) die Knochenlücken … bedeutend größer, plumper und dichter beisammen gelegen, und auch die Knochenkanälchen sind größer und verfilzen sich dicht durcheinander” (Koganei 1911:123-124). Similar information was also given by the Austrian pathologist Rokitansky (cf. Koganei 1911). Indeed, this description is what we would diagnose today as woven bone. Further information about these changes in macerated bones was given by Schultz (1993a).

Various kinds of meningeal diseases, such as epidural hematoma, meningitis, and meningoencephalitis produce characteristic vestiges on the endocranial lamina of the skull bones. Whenever newly built bone formations are visible, the pathological process represents a pachymeningitis. As in subadults, particularly in babies and infants, the dura mater has the properties of the periosteum and can react in a similar way. Thus, meningeal disease and the products of its reactions can be differentiated by microscopic investigation into hemorrhagic, inflammatory, and mixed forms (hemorrhagic-inflammatory or inflammatory-hemorrhagic). The internal lamina of the skull bones is rarely affected. However, in hemorrhagic processes and areas of the skull vault affected by a relatively large focus of meningeal inflammation, the characteristic impressions of atypical blood vessels can occur. Frequently, symptoms of increased brain pressure induced by the cerebrospinal fluid are observed. Further meningeal diseases can also be reliably diagnosed, for example, tuberculous meningitis (Leptomenigitis tuberculosa) and subdural empyema, as well as hemorrhagic

- **FIGURE 6-32** (a) Level one and (b) Level two line drawings, true to the original undecalcified thin ground sections (50 µm; frontal sections) through the frontal bone of a 5–7-year-old child from Boğazkale (central Anatolia), burial 37/83, early Byzantine period. In the impression of the sagittal sulcus, there are porotic plates (arrows) that represent vestiges of a hemorrhage. One of the plates covers the opening of a blood vessel canal (diploic vena). Magnification approximately 8x.
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FIGURE 6-34 Line drawing, true to the original undecalcified ground sections (25 μm), that demonstrate the development of severe epidural hematoma shown in a recent case in the parietal of a subadult individual from the historic collection of the Department of Pathology of the University of Göttingen (case GP-1985628; magnification approximately 1x). The original internal lamina was pressed by the hematoma into the diploë of the vault; secondarily, the skull vault was evidently thickened by the organized and transformed hematoma.

FIGURE 6-35 Line drawing, true to original undecalcified ground sections (25 μm), that demonstrates the development of severe epidural hematoma. Magnification approximately 1x. The comparable case from ancient times shows the right parietal bone of an approximately 5-year-old child from Ikiztepe (northern Anatolia), burial 181, Early Bronze Age. An epidural hematoma caused a relatively large and deep impression in the skull vault (arrows; cf. Fig. 6-65).

FIGURE 6-33 (a) Macroscopic view and (b) scanning-electron microscopic image of the endocranial surface of the right parietal bone of an 8-13-year-old child from Ephesus (western Anatolia), Late Byzantine Period. Blood vessel impressions mark the area of an epidural hematoma.

cases in which vestiges at the internal lamina of the skull vault demonstrate that such bleeding was organized during a certain healing process (Schultz 1993a; Carli-Thiele 1996; Kreutz 1997). For comparative purposes, an extreme case from recent times (historic collection of the Department of Pathology of the University of Göttingen) is presented that shows that the bleeding affected the parietal bone so badly that the hematoma caused a relatively large and deep impression in the skull vault of a subadult individual (Figure 6-34). The original internal lamina was pressed by the hematoma into the diploë of the vault. Vestiges of an advanced remodeling, represented by the morphological fusion of the primary and secondary bone trabeculae, are observable. The stage of healing is expressed by the transformation from soft to bony tissues (Figure 6-34). The paleopathological case was excavated at the Early Bronze Age cemetery of Ikiztepe (northern Anatolia). At the internal lamina of the frontal bone of an approximately 5-year-old child, remodeled vestiges of a characteristic epidural hematoma are situated (cf. Schultz 1993a). The sagittal cross section (Figure 6-35) shows the same structures as described, but the process was not as advanced as the first case. Also the microscopic morphology corresponds with the features of the recent case. It is interesting that a very few of the small structures inside the newly built formation that represents the original hematoma were necrotic (Figure 6-65).

The majority of cases dealing with meningeal reactions belong to a disease group that comprises mixed hemorrhagic and inflammatory components. Expressions of this kind of meningeal disease are usually characterized by fine, very short sinuous blood vessel impressions and very small, flat, stalked plates (Figures 6-36). An examination of thin ground sections, which reveal the latter changes responsible for an inflammatory process with polarized light, allows the paleohistopathologist to diagnose primitive or coarse woven bone (Figure 6-36b). Additionally, a scanning-electron microscopic investigation uncovers the stage of organization (i.e., of remodeling), which allows a prognosis on healing at the time of death. However, the stage of the healing process can also be estimated by light microscopy using polarized light (Figures 6-37b and 6-61).

Manifestations of tuberculous meningitis are characterized not only by the changes described (Figure 6-38), but also by relatively small, granular impressions that have diameters that vary between 0.5 and 1.0 mm (Figure 6-39 and 6-40). Microscopically, the lesions are very character-
Meningeal Reactions

FIGURE 6-36 Sagittal section through the frontal bone of a 2-3-year-old child from İkiztepe (northern Anatolia), burial 145, Early Bronze Age. (a) Line drawing, true to original undecalcified ground sections, that demonstrate the development of inflammatory reactions in the meninges. Very small, flat, stalked plates in pronounced digital impressions (arrows) are characteristic of an inflammatory meningeal reaction (probably bacterial meningitis). Magnification approximately 1×. (b) Microscopic view of undecalcified thin ground section (50 μm) viewed with polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25×. a = diploe; b = internal lamina; c = product of meningeal reaction.

FIGURE 6-37 Sagittal section through the occipital bone of a 12-18-year-old individual from Stillfried (Lower Austria), Late Bronze Age. (a) Line drawing, true to original undecalcified ground section, that demonstrates the development of inflammatory and hemorrhagic reactions in the meninges. Small irregular plates on the surface of the endocranial lamina (arrows) are the result of meningeal reaction (e.g., bacterial meningitis) associated with a severe hemorrhagic component such as scurvy or trauma.) Magnification approximately 2×. (b) Microscopic view of undecalcified thin ground sections (50 μm) viewed with polarized light using a red first order (quartz) hilfsobject as a compensator that show microscopic evidence of hemorrhagic and inflammatory meningeal reactions a = diploe; b = internal lamina; c = product of meningeal reaction. Magnification 25×. Structures are well organized, that is, the healing stage is represented by partly woven and partly lamellar bone.

Characteristic and a reliable indicator of Leptomenigitis tuberculosa, because in polarized light, the intra vitam origin of these impressions can be easily differentiated (Figure 6-39). The fact that these lesions could apparently be organized (remodeled) after a certain lapse of time (Figure 6-40) if a child could survive long enough is interesting. The localization of these impressions, which are generally grouped in clusters, is very characteristic. They are situated at the endocranial surface of the base, sometimes also at the lateral wall of the skull, especially in the middle and the posterior cranial fossa, and occasionally also in the cerebral fossa of the occipital bone (Templin 1993; Templin and Schultz 1994; Teschler-Nicola et al. 1994, 1996; Schultz 1999a, 2001b). They are caused by “pressure atrophy” of the tuberculars. They are a specific feature and are characteristic of this kind of tuberculous disease. If only the vestiges (Figure 6-38) are present, which are mainly characteristic of nonspecific meningeal reactions (e.g., inflammatory–hemorrhagic meningitis), tuberculous meningitis cannot be diagnosed.

Infant mortality in prehistoric and early historic populations often reached 40–60% or even more. Until recently, the causes of this exceedingly high mortality rate were, at the most, a matter of speculation. Recently, the results of a large project in paleopathological research using extensive microscopic investigations have demonstrated that inflammatory and hemorrhagic reactions of the meninges are among the most important factors that frequently led to death in infancy (Schultz 1993a). Thus, the role of meningeal diseases in the mortality of infants and children in prehistoric and historic populations was, until recently, frequently underestimated.
FIGURE 6-40 Sagittal section through the frontal bone of a 6-10-year-old infant from Bettingen (Switzerland), Ind. 2076-1, Late Middle Ages. The granular impression was caused by pressure atrophy induced by a tubercle. Vestiges of healing are shown in the original wall of *intra vitam* originated impression (arrows). The impression is partly filled by newly built bone (coarse woven bone). The remodeling process was not finished because the infant died. There is microscopic evidence of tuberculous meningitis. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 100x.

**FRACTURE OF SKULL VAULT AND CONCOMITANT PHENOMENA**

In conjunction with a skull trauma, the bones of the vault can break. If the patient survives, callus builds up and develops into woven bone. Callus in archeological bones rarely has been examined by microscopic techniques (cf. Schultz and Teschler-Nicola 1984, 1987c). As an example, the skull vault of a recent mature individual (historic collection of the Department of Pathology of the University of Göttingen) was selected. The vault was broken in the region of the right parietal and both fractured parts overlapped in the fracture line (Figure 6-27a). The broken parts were already fused together in this situation (Figure 6-27c). Thus, callus produced at the ectocranial and the endocranial surfaces of the vault had already started to be transformed to woven bone when this person died. In the region next to the fracture line, new bone formations were found at the endocranial lamina that were probably also built up by the meninges (Figures 6-27a and d). The micromorphology of the callus and the other newly built formations (cf. Figures 6-27a and d) shows that the new bone trabeculae are very gracile and represent only primitive woven bone. Thus, the organization (i.e., bone remodeling) was not very advanced. Therefore, these structures are difficult to diagnose. Microscopically, the new bone formation at the endocranial surface of the right parietal bone, situated relatively close to the fracture line (Figure 6-27a, feature b), can be seen to have a morphology similar to that found in a circumscribed...
epidural hematoma. Here, in contrast to a single-layered subperiosteal hemorrhagic process at the external surface of a long bone (cf. Figure 6-29), the newly built bone trabeculae (woven bone) are oriented parallel to the internal lamina and suggest at least two layers (Figure 6-27d). These findings contrast with multilayered structures found as the product of inflammatory processes at the endocranial surface of the skull vault. Here, in general, the bone trabeculae are mainly oriented perpendicular to the internal lamina (cf. Figure 6-60). The platelike new bone formation at the endocranial surface of the frontal bone (Figure 6-27b) macroscopically resembles a bony membrane covering a pathological process (e.g., hemorrhage). Inside this plate, the structure consists of relatively densely packed bone trabeculae (Figure 6-66). It is important to keep in mind that primarily induced inflammatory or hemorrhagic processes of the meninges that demonstrate a more advanced stage of organization show different morphological structures at the microlevel (cf. Figures 6-36b, 6-37b, 6-41a and b, and 6-61).

**PRIMARY INFLAMMATORY PROCESSES OF THE PERICRANIUM AND SKULL VAULT**

Sometimes, an inflammatory process of the scalp can affect the external surface of the skull vault. After healing, characteristic vestiges are visible. A 7–9-year-old child from Byzantine Pergamon (western Anatolia) shows a coarse and cicatricial surface in both parietal bones, between the two temporal lines, that is characterized by several short, slightly branching blood vessel impressions, some of which are relatively deep and have a starlike configuration (Figure 6-42a). As the microscopic investigation demonstrates, these lesions are of *intra vitam* origin and represent an inflammatory process that healed by cicatrization (e.g., slitlike impressions representing scars; cf. Figure 6-42b). The blood vessels that caused the impressions originated during the healing process by which the skull vault was slightly thickened (Figure 6-42b).

It is well known that inflammatory processes that affect the skull look, in the macerated specimen, very similar in their macroscopic morphology. Only the changes caused by treponemal diseases sometimes constitute an exception (cf. Hackett 1976). However, particularly for the inexperienced paleopathologist, it is not easy to establish a correct diagnosis. In these cases, microscopic investigation can help. It is striking that, as a rule, the morphological changes caused by different inflammatory diseases are really different at the microlevel. Thus, characteristic cases are presented.

After a skull trauma, an inflammatory process can develop that affects the red blood marrow (diploë) of the skull vault. Thus, a nonspecific osteomyelitic process destroys the bone substance of the vault in a relatively short time, similar to what is seen in long bones. This characteristic was demonstrated in a recent case (historic collection of the Department of Pathology of the University of Göttingen). The section through the left part of the frontal bone of a senile person reveals severe osteoclastic destruction and secondary new bone formations that are scattered irregularly between the edges of the remaining bone trabeculae (Figure 6-43a). The microscopy makes the relatively discrete osteoblastic activity visible (Figure 6-43b). For comparison purposes, an archeological case (cf. Teschler-
FIGURE 6-42 Inflammatory process of the scalp in a fragment of the left parietal bone of a 7–9-year-old child from Pergamon (western Anatolia), burial 14F, Late Byzantine Period. (a) Macroscopically, the coarse and cicatricial surface is characterized by several short, slightly branching blood vessel impressions of which some are relatively deep and have a starlike configuration centering to slitlike impressions (scars). (b) Sagittal section. The skull vault is slightly thickened (darker area with small holes represents the secondary external lamina that was built up by an inflammatory process). The relatively deep impression represents a scar (arrow). Undecalcified thin ground section (50 µm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 25x.

Nicola and Schultz 1985) is presented that demonstrates the same changes (Figure 6-44). Sometimes, osteomyelitis of the skull vault is also seen in the skulls of subadults. Here, the changes can be very dramatic (cf. Figure 6-45).

In contrast, a tuberculous process of the skull vault represents a much more slowly developing process. Thus, the destruction is, as a rule, not as excessive. However, tuberculosis of the skull bones also can damage the skull
Primary Inflammatory Processes of the Pericranium and Skull Vault

FIGURE 6-43 Frontal bone of a recent senile individual (historic collection of the Department of Pathology of the University of Göttingen; case GP-1985901) that shows excessive osteolytic processes with secondary remodeling and nonspecific osteomyelitis after skull trauma. (a) Line drawing, true to original undecalcified ground section (25 μm), that demonstrates features of inflammatory skull diseases. Magnification approximately 1×. (b) Microscopic features in nonspecific inflammatory processes of the skull vault. The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator, a = external lamina; b = newly built bone trabeculae in the diploë. Magnification 25×.

FIGURE 6-44 Archeological skull of a juvenile female from Guntramsdorf (lower Austria), Ind. II, Iron Age (La Tène B) Celtic Culture: a = external lamina; b = newly built bone trabeculae in the diploë; c = osteolytic lesion on the external lamina of the skull vault due to inflammatory process caused by trauma (cf. Teschler-Nicola and Schultz 1985; trephination). The undecalcified thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Magnification 22×.

FIGURE 6-45 Porotic hyperostosis in the subadult skull vault. (a) Line drawing, based on original undecalcified ground sections of a vault fragment of a 6–12-month-old infant from the pre-Columbian Sundown Site (USA), burial 12. The skull vault was severely destroyed by nonspecific osteomyelitis. Periostitis on the eocranial and endocranial surfaces caused new bone formations represented by gracile, more or less irregularly oriented bone trabeculae that branch frequently. Most of the diploic trabeculae were eaten away by the inflammatory process. Magnification approximately 2×. (b) Microscopic features of porotic hyperostosis in the skull of this case. The undecalcified sagittal thin ground section (50 μm) was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. Severe nonspecific osteomyelitis of the skull vault accompanied by periostitis, is evident. There are new bone formations = a on the external lamina = b. The diploë is almost completely lysed = c. On the internal lamina = d, there are extremely well developed bone formations = e. Magnification 25×.

severely, but in a different way, particularly at the microlevel. To illustrate, again a recent case is presented (historic collection of the Department of Pathology of the University of Göttingen). In the frontal bone of an adult individual, a perforation (necrosis) took place close to the coronal suture and due to the tuberculous process (Figure 6-41a). Only in the closely adjoining region of this perforation was the bone affected by an excessive remodeling process during which the external and the internal laminae as well as the diploë were completely transformed to irregular, dense woven bone (Figure 6-41a, c and d). There are distinct vestiges of osteoclastic resorption (Figure 6-41a and c). Additionally, the meninges were affected as is characteristic of a hemorrhagic–inflammatory meningitis (Figure 6-41a and b). Overall, the changes in tuberculous bone disease are apparently completely different at the microlevel from nonspecific osteomyelitis.

As a rule, changes caused by tertiary syphilis (venereal syphilis) in the skull vault look, at the microlevel, very
different from what is seen in nonspecific osteomyelitis and tuberculous disease. To illustrate this and the uniformity of bone changes in tertiary syphilis of the skull vault, a series of six recent cases is demonstrated (Collection of the Institute of Legal Medicine of the University of Vienna and the historic collection of the Department of Pathology of the University of Göttingen). All these cases were collected between the end of the 19th and the first half of the 20th centuries. The sections presented in Figures 6-46a to 6-50a describe the advanced development of morphological destruction of the skull vault to various degrees (cf. Hackett 1976). The series starts with a relatively severe osteolytic destruction of the external vault due to a florid process (Figure 6-62) that develops into the characteristic radial scar (Figure 6-46a). Such a lesion can enlarge to an elongated depression (Figure 6-47a) that can lead to small, nodular cavities in the diploë (Figure 6-48a). Sometimes, the depressions can be remodeled by the building of secondary woven bone and appear as scars with remodeled rims (Figure 6-49a).

FIGURE 6-47 Syphilitic lesions of the skull. (a) Line drawing of the right frontal bone of an adult. The drawing is true to the original undecalcified ground sections that show the manifestations of advanced venereal syphilis (tertiary stage) in the skull vault, including enlargement of an elongated depression. Magnification approximately 1x. (b) Right parietal bone of the same individual showing remodeling of a depression and nodular cavities reduced in size but still in place. Collection of the Institute of Legal Medicine of the University of Vienna (case RMW-Sch5).

FIGURE 6-48 Syphilitic lesions of the skull. (a) Line drawing, true to original undecalcified ground sections, of the left parietal bone of an adult with advanced venereal syphilis (tertiary stage). There are nodular cavities in the diploë and the section demonstrates the morphological uniformity of this disease at the microlevel. Magnification approximately 1x. (b) Microscopic features of the tertiary stage of venereal syphilis of the skull vault. The undecalcified thin ground section (50µm) of the left parietal was viewed through the microscope in polarized light using a red first order (quartz) hilfsobject as a compensator. This section demonstrates the growth of the nodular cavity by osteoclastic reaction (Howship’s lacunae denoted by arrows) in primary diploë. Historic collection of the Department of Pathology of the University of Göttingen (case GP-1985689). Magnification 25x.
Syphilitic lesions of the skull. (a) Line drawing, true to the original undecalcified ground section, of advanced venereal syphilis (tertiary stage) in the left parietal bone of an adult skull vault that demonstrates the morphological uniformity of this disease at the microlevel. "Healing" is seen in the form of a flat depression with a coarse bottom. Magnification approximately 1x. (b) Microscopic features in the tertiary stage of venereal syphilis of the skull vault. Undecalcified thin ground section (50 µm) of the right parietal bone was viewed through the microscope in polarized light using a red first order (quartz) hñlsoñbject as a compensator. This section reveals a relatively smooth external surface in the region of the flat depression. Collection of the Institute of Legal Medicine of the University of Vienna (RMW-Sch2). Magnification 25x.

A temporary "healing" is possible in the form of a flat depression with a coarse bottom (Figure 6-49a) or as a pronounced thickening of the affected area of the vault with a relatively smooth surface (Figure 6-50a). In all of these stages of an advanced course of tertiary syphilis of the skull vault, an excessive transformation of the original structures of the vault bones into a sclerotic, very dense secondary bone structure is seen, which is predominantly represented by woven bone. Additionally, the meninges are frequently affected. The changes are similar to those observed in tuberculous skull diseases (Figure 6-46b; cf. Figure 6-41b). Before the syphilitic process affects the meninges, the internal skull lamina must be destroyed by osteoclastic activity (Figure 6-46b). Furthermore, there are some characteristic details that emphasize the foregoing features. Very aggressive, osteolytic foci at the external skull surface (Figure 6-62) are apparently characteristic of the tertiary stage of venereal syphilis (cf. Hackett 1976; Schultz 1986). The growth of the nodular cavities inside the diploe occurs after excessive osteoclastic destruction (Figure 6-48b). The degree of the healing in the region of the superficial scars can be clearly observed by microscopic investigation (Figures 6-49b and 6-50b).

In comparison to skull tuberculosis (Figure 6-41b–d) the changes in advanced tertiary syphilis are, as a rule, much more excessive and invasive. The changes are completely different from what is observed in nonspecific osteomyelitis of the skull vault (cf. Figures 6-43 and 6-44). For differential diagnosis, postmortem changes must be excluded (Figure 6-51; see pseudopathology).
Porotic hyperostosis of the skull vault (Cribræ cranii externa) and the orbital roof (Cribræ orbitales) is often seen in prehistoric infant skulls from all over the world (cf. Figures 6-52 and 6-53). In general, these changes are seen in subadults more frequently than in adults. On the basis of differential diagnoses and the etiology of diseases, we know that porotic changes on the external surface of the skull vault are sometimes associated with porotic changes on the orbital surface of the eye socket. Many North American scientists assume that porotic hyperostosis of the skull vault and the orbital roof are caused by anemia, especially by iron deficiency anemia (e.g., El-Najjar et al. 1976; Taylor 1985; Ubelaker 1992). However, recent paleopathological investigations have established (Schultz 1993a) that such morphological changes could also have been caused by various other diseases (see Table 6-2). Thus, following healing of inflammatory processes of the skull bones, for instance, periostitis, osteitis, and osteomyelitis (Schultz 1986, 1987b, 1990, 1993a; Kreutz 1997; Schultz et al. 2001), as well as inflammatory processes of the scalp (see preceding text and Schultz 1993a, Schultz 2001b), a porotic external surface of the skull vault can develop that is usually thickened. Such diseases can result from local primary inflammatory processes, frequently from head trauma or a scalp infection. It can also be the result of a secondary spread of inflammatory processes of the nasal cavity, the paranasal sinuses, or the orbit. Then, the primary focus can easily be detected by endoscopic investigation. Hemorrhagic processes on the external lamina, such as ectocranial hematoma (Wadsworth 1992; Schultz and Merbs 1996; Schultz et al. 1998; Teegen and Schultz 1999), can also involve the external skull surface when the bone stimulated by a hemorrhage has become remodeled to show a porotic nature. In these cases, seen more frequently in subadults, the skull vault is usually thicker than in healed inflammatory processes. In babies, the most common cause of ectocranial hematoma is trauma (e.g., cephalohematoma, caused by birth). Subadults who suffer from scurvy generally show a higher frequency of hemorrhagic processes. Further diseases, for example, tumors (e.g., hemangioma and meningioma) or even rickets (e.g., Schultz 1987b, 1993a; Carli-Thiele 1996; Kreutz 1997; Schultz et al. 1998; Schultz et al. 2001; Teegen and Schultz 1999), can be responsible for porotic hyperostosis. It should be remembered that the etiology of these processes and their interdependence are very important for a reliable reconstruction of the state of health and disease, and the physical condition of people of ancient times (Schultz 1982, 1996, 1999b).

Porotic hyperostosis of the skull vault and cribra orbitalia are not characteristic of a specific disease, but rather they represent a symptom of several diseases. Therefore, reliable diagnoses of these alterations can only result from careful investigation. Macroscopic and radiological investigation alone may not be sufficient because the macroscopic morphology of the structures of hyperostotic and porotic newly built bone formations caused by various diseases often looks the same. In addition, a molecular biological investigation is able to provide helpful diagnostic criteria for identifying anemic diseases (Faerman et al. 2000a, b).

The phenomenon of porotic hyperostosis in chronic anemia is characterized by two morphological features that usually are seen together and reflect the development of the following alterations (cf. Figures 6-52 and 6-53): (1) thinning of the external lamina, which creates the porosity because the cancellous bone (diploë) becomes visible, and (2) enlargement of the cancellous bone by radial growth of the bone trabeculae, which eliminates the external lamina by active remodeling stimulated by hematopoietic marrow hyperplasia and results in pressure atrophy. During the early stages of this process, only the external lamina becomes porotic and the growth of the diploë cannot be seen by macroscopic analysis in the early stages of the disease.
The different stages in the development of porotic hyperostosis in the skull of subadults caused by anemia (Figures 6-52 and 6-53) have been described (Schultz 1982, 1986, 1993b, 2001b).

In the first stage, the superficial vault surface is slightly porotic in the form of a fine, regular pitting that is only seen in very small, circumscribed areas. These changes are frequently found in the region of the parietal and sometimes also in the region of the frontal tubera, as well as in the occipital margin of the parietal bones where the porotic changes stretch ribbon-like parallel to the lambdoid suture. In the ground section, the external lamina of the affected regions is thin, already reduced, and even disintegrated. Additionally, the trabeculae of the diploë start to change from the original tangential to radial or perpendicular growth. In the second stage, the area of the porotic skull surface is enlarged and the pitting is more irregular, because the holes are larger and start to conflow. In addition to the areas mentioned previously, in this stage, the middle region of the occipital squama as well as some other areas of the vault can be affected. In the ground section, the external lamina is disintegrated in a larger area and the trabeculae of the diploë are clearly orientated in radial or perpendicular direction. Now, the so-called hair-on-end phenomenon (e.g. Steinbock 1976; Ortner and Putschar 1985; Aufderheide and Rodriguez-Martin 1998) starts to develop, causing a very slight thickening of the skull vault. As a rule, this slight thickening is very difficult to observe from outside. The external modules of the red bone marrow are enlarged because the affected skull bone grows only in the area of the external diploë. In the third stage (Figure 6-52), the affected area of the skull vault has thickened markedly. The holes responsible for the porosity are now also clearly enlarged. In the ground section, the trabeculae of the diploë take on a parallel orientation. Thus, the hair-on-end phenomenon has fully developed. As a rule, the relatively thick and bulky trabeculae are not very long. In this stage, the skull vault has changed in the affected region to a morphological feature that is called porotic or spongy hyperostosis. The last and fourth stage, which is rarely seen (Schultz et al. 2001), is characterized by a much more advanced thickening of the affected areas (Figure 6-53). The large holes superficially situated in the centers of the thickened areas of the tubera are confluent, and form space and labyrinth-like structures. In the ground section, the trabeculae between the enlarged modules of the red bone marrow are relatively long and thin (Figures 6-54 and 6-55). In all stages of anemic changes in the skull bones, the diploë surface of the internal lamina is only slightly or not at all involved (Figures 6-52 and 6-53). As a rule, the trabeculae in the thickened part of the vault are oriented in parallel direction, which produces the radial arrangement known as the hair-on-end phenomenon (cf. Steinbock 1976). These changes can heal. Thus, the modules of the red bone
marrow toward the external bone surface can be remodeled secondarily. Then, at the edges of the porotic areas, vestiges of a remodeling process are seen that are caused by a secondary change in the bone structure of the vault. These can be interpreted as the result of "partial healing."

Very often, macroscopic alterations characteristic of such an advanced stage of porotic hyperostosis due to anemia are very similar to changes caused by scurvy or hemangioma (extremely rare). However, the changes typical of advanced stages of rickets and inflammatory diseases (e.g., inflammatory processes of the scalp, periostitis, osteitis, and osteomyelitis of the skull vault) are usually different in morphology. Thus, a reliable diagnosis is not difficult to make. For comparison purposes, a characteristic case of an ectocranial subperiosteal hematoma due to chronic scurvy is presented (Schultz and Merbs 1996). The skull vault of an infant from the pre-Columbian Sundown Site (Arizona, USA) macroscopically shows the phenomenon of pronounced porotic hyperostosis that reasonably leads to a tentative diagnosis of anemia. However, the microscopic research reveals features of changes (Figure 6-56) due to a hematoma first organized as fibrous connective tissue and then converted to woven bone. For differential diagnoses, one must be aware that a subperiosteal hematoma is situated on the original bone surface (Figure 6-56b) and does not affect large areas of the external lamina (see preceding discussion on productive reactions), and, furthermore, that the diploë has a normal structure. In addition, a typical hair-on-end phenomenon, as pronounced as in long existent chronic anemia, is not generally seen in a subperiosteal hematoma of the skull bones. Sometimes though, in relatively discrete cases, porotic hyperostosis caused by hematoma, anemia, and sometimes by rickets is very similar. Here, the criteria described previously (structures that involve the external lamina and the diploë) help to establish the correct diagnosis. Chronic vitamin C deficiency is the most frequent cause of subperiosteal hematoma in subadults; therefore, the probable diagnosis is scurvy (for additional criteria, see Schultz 1988–1989, 1990; Schultz and Schmidt-Schultz 1995; Schultz et al. 1998).

As already mentioned, chronic rickets can also produce porotic hyperostosis, but, to a relatively slight degree. Two typical cases are presented. The first skull of a child (age group Infans II, 7–14 years) is a recent case (historic collection of the Department of Pathology of the University of Göttingen). The skull bones are remarkably thickened, particularly in the area of the frontal and parietal tubera. The bony trabeculae of the diploë are gracile and show a special pattern that is due to the reduced structure of the modules of the red bone marrow (Figure 6-13). In the affected areas, the skull surface shows a coarse porotic structure. Here, the bone trabeculae are very gracile and have built up rachitic osteophyte that is structured as an osteoplaque (Figure 6-13). Very similar changes are seen in the skull of a newborn to 3-month-old infant. Macroscopically, the porotic vault is only slightly enlarged (Figure 6-14). The results of the microscopic investigation indicate rickets and clearly exclude anemia, scurvy, and inflammatory processes because of the characteristic microscopic features described earlier.

Additionally, a case of osteomyelitis of the skull vault is presented for comparison purposes. The skull of a young infant from the pre-Columbian Sundown site has a large area of bone apposition on its external surface (Figure 6-45a). Microscopically, all features support the diagnosis of osteomyelitis of the skull vault (Figure 6-45b).

Furthermore, there are other diseases that are also expressed by an excessive thickening of the skull vault such as osteitis deformans (Paget's disease). Here, the original morphology of the bones of the skull vault, which are the external and internal laminae and the diploë, are completely changed (Figure 6-25) and remodeled by the formation of small trabecula-like formations that look like fragments characteristic of this disease (Figure 6-26). Microscopically,
these trabeculae sometimes show a certain mosaic structure (Figure 6-26).

Finally, there are thickened skull vaults that cannot be grouped into the classes described. Such a case is presented in Figure 6-57. The cranium of a mature male from the Iron Age of Yugoslavia shows a remarkable thickening of the whole vault (cf. Schultz 1993a). The man suffered from *Pachymeningeosis haemorrhagica interna* and was the subject of surgery during his lifetime (three holes made by a conical drill). He survived this surgical event, which was probably repeated twice, for many years. Microscopically, the thickening was caused by a process of the meninges that cannot be classified in detail (hemorrhagic?) and that stimulated the growth of the vault surface toward the brain (Figure 6-57).

All the foregoing descriptions of porotic changes of the skull vault can similarly be observed in the orbital roof. In general, only a histological examination yields reliable results (Schultz 1987b, 1993a, b; Wapler and Schultz 1997; Wapler 1998; Schultz et al. 2001). Even if it is difficult for the paleopathologist working macroscopically to accept, macroscopic study of the external morphology of porotic orbital roofs will only rarely lead to a reliable diagnosis. Therefore, without microscopic analysis, paleopathologists should restrict their assessment of porotic hyperostosis of the skull vault and the orbital roof to stress indicators and not try to diagnose specific diseases, such as iron deficiency anemia (Schultz 1993b, 2001b; Schultz et al. 2001). Here, as characteristic examples, two cases of porotic hyperostosis of the orbital roofs are described (cf. Schultz 2001b). The ground sections of porotic and thickened orbital roofs of a 2-year-old infant from the Early Bronze Age at the Ikiztepe (northern Anatolia) site show the classical features of hypertrophy of the red bone marrow. The modules of the red bone marrow are longitudinally enlarged, the bone trabeculae are oriented parallel (hair-on-end phenomenon), and the orbital lamina is completely reduced *intra vitam*. The other case is a 4–6-year-old child who lived in the early Middle Ages at Hailfingen (southern Germany). Here, the orbital roof is only slightly thickened, but has a porotic surface. These features were produced by a hemorrhage, but could also have been due to a hemorrhagic-inflammatory process in the orbit that created the new bone formation similar to the process already described for proliferative reactions on the surfaces of long bones.

Some practical applications are now presented that demonstrate the advantage of diagnoses based on reliable microscopic techniques. There are various reasons why subadults suffered from anemia. The most frequent etiologies are parasitic disease (e.g., Reinhard 1992; Larsen and Sering 2000), chronic iron deficiency, for example, caused by lack of iron in the diet (e.g., El-Najjar et al. 1976), thalassemia (e.g., Ascenzi et al. 1991), or chronic malnutrition, such as chronic deficiency of the amino acid tryptophan (Schultz 1982). More detailed information was given by Garn (1992).

Chronic vitamin C deficiency is an important factor of morbidity and mortality in prehistoric populations (e.g., Steinbock 1976; Maat 1982; Holck 1984; Ortners and Putschar 1985; Außerheide and Rodríguez-Martin 1998). It is well known that scurvy, particularly in subadults, is accompanied by widespread subperiosteal bleeding, which can be diagnosed in archeological skeletal remains because of the characteristic newly built bone formations and, additionally, vascular porosity, which is also found in inflammatory processes. However, the diagnosis of chronic scurvy in archeological skeletal remains by microscopic analysis alone may be unreliable. Whereas subperiosteal bony structures are also caused by various other diseases such as inflammatory processes, microscopic investigations may be necessary. In dry bones, the main features caused by chronic scurvy are subperiosteal new bone formations that represent mineralized hemorrhagic processes. Such alterations are frequently found in the shafts of the long bones, in the skull vault, and in the jaw area. In subadults, these pathological changes are usually much better expressed because bone growth is more active in this age group. There is a close connection between scurvy and other diseases such as posthemorrhagic anemia. Additionally, scurvy may contribute to a secondary immunodeficiency (Schmidt-Schultz and Schultz 2001). Thus, infectious diseases may be a complicating factor in scurvy.

**Pseudopathology**

Now that we have discussed examples of specific morphological features characteristic of particular diseases and some basic bone reactions with which we can elucidate the
mechanisms of bone behavior during pathological processes, an understanding of pseudopathological changes might be easier to gain. We briefly mentioned pseudopathology in the section about decomposition and diagenesis. Following discussion of the mechanisms of *intra vitam* proliferative reactions, we can easily differentiate between these lesions and postmortem changes that simulate pathological alterations. In 1967, Wells introduced the term pseudopathology. It is often difficult to differentiate macroscopically between the effects of diseases and postmortem changes in archeological bones, especially when the skeletal remains are poorly preserved (Schultz 1986, 1997b). Furthermore, the histopathological analysis of poorly preserved bones can create serious problems in disease diagnosis. There is a characteristic case in an 8–10-year-old child buried at the Early Bronze Age cemetery from Ikiztepe, northern Anatolia. The lingual surface of the left part of the mandible of this child has a newly built bone formation that appears to be a periosteal reaction due to an inflammatory process. However, microscopic analysis in polarized light reveals a postmortem apposition that consists of broken bone trabeculae, probably from the visceral cranium, that accumulated build up of secondary crystals at the lingual surface of the mandible.

Occasionally, traces are observed that look macroscopically like vestiges of a pathological process; however, microscopic analysis can prove their postmortem origin (Figures 6-3 and 6-51). There are also features that initially look like postmortem conditions and then turn out to be the result of *intra vitam* processes. In metastatic carcinoma, for example, the eroded structures look like postmortem changes, but can be proved to be the result of osteoclastic resorption by scanning-electron microscopic analysis and light microscopic examination of thin ground sections. These typical features of *intra vitam* resorption are characterized by masses of Howship’s lacunae on bone surfaces, the irregular shape of bone trabeculae, and the margins and edges of resorption holes, where osteoclasts have eaten away the bony substance (Figure 6-12). Finally, also the results of technical problems (e.g., air bubbles between the sample and the coverglass) can simulate vestiges of disease or diagenesis (Figure 6-58).

**CONCLUSIONS AND SUMMARY**

In the interdisciplinary field of paleopathology, various methods, including macroscopic, radiological, and endoscopic methods, are required to which microscopy should be added. In this chapter, this necessity has been highlighted by specific examples of disease, such as anemia, scurvy, meningeal reactions, and nonspecific and specific osteomyelitis including venereal syphilis. Selected examples of mechanisms of pathological bone changes have been presented, dealing mainly with proliferative reactions in the periosteal area of long bones, the meningeal reactions of the endocranial surface of the skull, inflammatory processes of the skull vault, and the porotic hyperostosis of the skull vault and corresponding changes on the orbital roof (cribra orbitalia). It has been demonstrated that the histological investigation of archeological skeletal remains indeed provides greater reliability in establishment of diagnoses in some cases. The pattern of the architectural changes in the cortical, compact, and spongy bone substances, particularly in the newly built bone formations, provides an effective key with which to establish a diagnosis. Therefore, special categories have been presented to make the process of diagnosis easier. Thus, we have morphological features at the microlevel, such as faserfilz osteons (in slowly growing primary osteoblastic bone tumors), grenzstreifen, and polsters (in chronic treponemal diseases; apparently also in chronic leprosy in only a slight modification), that are important indicators of particular diseases or groups of diseases. Furthermore, there is evidence of basic bone reactions that characterize bone behavior also at the microlevel, such as proliferative (productive and osteoblastic) and osteolytic (osteoclastic) reactions. Finally, we see morphological symptoms (e.g., thinning or thickening of the external lamellae of the skull vault and enlargement of the diploë) that can be grouped into morphological syndromes, such as porotic hyperostosis or cribra orbitalia. These syndromes do not represent or characterize one particular disease but can be caused by various diseases.

For microscopic analysis of ancient bones, a good working knowledge of the microscopic structure of bone, including the histogenesis and growth of bone, as well as of the influences of decomposition and diagenesis, which help
to avoid false diagnoses due to pseudopathology, is indispen-
sable. The method of choice is the study of dry bone
samples by thin ground sections. To investigate thin ground
sections using plane or polarized transmission light, a
special embedding technique is required for the fragile and
sometimes poorly preserved bone samples. Additionally,
the thin ground sections must be technically well produced.
For these purposes, special techniques have been developed
(Schultz and Drommer 1983; Schultz 1988). However, suit-
able techniques alone are not enough: experience and a
collection of specimens for comparison purposes are neces-
sary to establish reliable diagnoses. False diagnoses based
on postmortem changes such as those due to diagenesis are
avoidable. Additionally, microradiography and scanning-
electron microscopy are powerful tools for diagnosing
ancient bones.

It is important to be aware that it is possible to establish
a general diagnosis from archeological bone samples by
microscopic research and, in many cases, also differential
diagnoses, even though soft tissues and cells, which are the
most important features in recent pathology, are no longer
present. The etiology and epidemiology of ancient diseases
require reliable diagnoses as the basis of further research.
Thus, a paleohistopathological examination of archeological
skeletal remains should be part of the methodological arsenal
of every paleopathologist.

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