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Pneumatization of the temporal bones and otitis media in ancient and modern Greenlanders

Preben Homøe

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Otitis media occurs frequently among modern Greenlanders. However, knowledge of the epidemiology of this disease before the twentieth century is scanty. Information on diseases in the past may give us a better understanding of the health of historical populations. This study presents a new unbiased method for estimating the incidence of infectious middle ear disease (IMED) in childhood. The method is based on the relationship between IMED in childhood and morphological evidence present in the human temporal bones – i.e. small or asymmetrical pneumatized cell areas.

In a standardized X-ray projection, we examined 434 pneumatized cell areas in temporal bones from 34 living adult modern Greenlanders, 56 historical adult Greenland Eskimo crania from the period after the European colonization of Greenland in 1721 AD, and 127 prehistoric adult Greenland Eskimo crania from the period before the colonization. The resulting X-rays of the crania were of high quality and the relationship between IMED in childhood and small or asymmetrical pneumatized cell areas was confirmed in the modern Greenlanders. On this basis a polychotomous logistic regression model was applied to the pneumatized cell areas of the three groups of material. The model allowed for the interdependence of the ears and specified probabilities of having IMED in the right ear, left ear, both ears or of being healthy in both ears.

The frequency of IMED as indicated by the model was 8/34 (23.5%) in modern Greenlanders, 10/56 (17.9%) in historical Eskimo crania and 6/127 (4.7%) in prehistoric Eskimo crania ($p < 0.002$). The mean area also differed significantly, as it was smallest in modern Greenlanders. The results thus indicated a change in the frequency of IMED and a decrease in area from historical to present-day Greenland in subjects who survived to adulthood. The change seemed closely related to the European colonization of Greenland. As IMED is closely related to upper respiratory tract infections and to poverty, the method seems well suited for evaluating general health in past societies.

Keywords: Otopathology, Palaeopathology, Physical anthropology, Epidemiology, Palaeoepidemiology, Archaeology, Ethnology, Inuit, Arctic, Otitis media, Upper respiratory tract infections, Polychotomous logistic regression.

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Introduction

Otitis media (OM) is a common disease all over the world and is closely related to episodes of upper respiratory tract infections (URI) which often precede OM (Branefors-Helander et al. 1975; Henderson et al. 1982; Tos et al. 1984). In some parts of the world and in some indigenous peoples such as the Eskimos of the Arctic, the Aboriginals of Australia, the Maoris of New Zealand, the Polynesians and others, OM constitutes a frequent major health problem causing chronic ear discharge and often hearing impairment (Ling et al. 1969; Reed and Dunn 1970; Maynard et al. 1972; Baxter and Ling 1974; Manning et al. 1974; Baxter 1977, 1983; Wiet et al. 1980; Sunderman and Dyer 1984; McCafferty et al. 1985; Baxter et al. 1986; Pe-

dersen and Zachau-Christiansen 1986, 1988). Various explanations have been put forward, including sociomedical and anatomical arguments (Schaefer 1971; Ratnesar 1976; Doyle 1977; Baxter 1982, 1983; Todd 1983; Bastos 1994). However, none has proven convincing as a unique explanation, and a combination of the above factors, including genetic and immunological factors, is most likely.

The history of diseases in indigenous populations before contact with western culture is almost unknown. Knowledge of the palaeopathological disease pattern in these populations may provide new information on the aetiology, pathogenicity and pathophysiology of certain diseases. Studies of OM in ancient populations may provide information on the health and social welfare of ancient populations, since several modern studies have found that OM is associated with poor social and housing conditions (Christensen 1956; Berg and Adler-Nissen 1976; Vinther et al. 1982; Bastos 1994). Such information may in turn help archaeologists to describe the living conditions of past societies. As OM is one of the main health problems in Greenland today, it was natural to try to examine whether OM was also a major health problem in ancient Greenland.

The Laboratory of Biological Anthropology at the Panum Institute in Copenhagen houses a large computer-registered sample of skeletal material from the Greenland Eskimos, comprising almost 1500 individuals (Lynnerup et al. 1992a). The material represents skeletal remains from different periods and from different regions of Greenland. The skeletal remains have been collected over the last 100 years, mostly in archaeological excavations while some were random finds.

Abbreviations

OM	otitis media
COM	chronic otitis media
CSOM	chronic suppurative otitis media
CTD	chronic tubal dysfunction
AOM	acute otitis media
RAOM	recurrent acute otitis media
SOM	secretory otitis media
IMED	infectious middle ear disease
URI	upper respiratory tract infection
W	west coast of Greenland
SE	south east coast of Greenland
NE	north east coast of Greenland
CI	confidence interval

Hypothesis, objectives and structure of the thesis

The hypothesis of this study is that it is possible to estimate the frequency of OM in ancient populations by studying the pneumatized cell area in the temporal bones. This was done by using the skeletal material from Greenland Eskimos and a sample of living Greenlanders. The objectives of the study were:

1. to estimate the frequency of infectious middle ear disease (IMED) in ancient Greenland Eskimos compared with the high frequency of IMED in the Eskimos of modern Greenland;
2. to study the distribution of temporal bone pneumatization in Greenland Eskimos with special reference to sexual dimorphism, cranial morphology and spatial and diachronic variance;
3. to establish a standard method for making unbiased estimates of the frequency of IMED in ancient populations on the basis of modern medical research. This may be of importance to archaeologists in reconstructing the health and social conditions of ancient populations.

Since pneumatized cell areas had not been measured before in ancient anthropological material, and since most of the important studies of temporal bone pneumatization had been carried out on living whites, it was necessary to do a series of studies. The project was thus divided into phases as described below:

I. The first study was a pilot study attempting to determine the distribution and size of the pneumatized areas, including the degree of asymmetry in skeletal material from Greenland Eskimos. Certain procedures were used to validate the accuracy and repeatability of the technique, and included tests for inter- and intraobserver variation. The crania were aged and sexed using routine anthropological procedures. Since the size of the pneumatized cell area may be influenced by cranial morphology, the study included screening for possible correlations between the pneumatized area, cranial size and sexual dimorphism.

II. The aim of the second study was to validate the results of the first study by performing otomicroscopy and CT scanning of the crania suspected of having had IMED.

III. The aim of the third study was to characterize the relationship between IMED and pneumatization in living Greenlanders, since this relationship has only been established in whites. This was necessary in order to develop a model for estimating the frequency of IMED which was based not only on the pneumatized cell area itself, but also on the extent of asymmetry, with due consideration for the interdependence between single ear pairs. The model was subsequently applied to the anthropological material consisting of Greenland Eskimo crania used in the first study.

IV. The objectives of the fourth study were to investigate the frequency of IMED and the distribution

of pneumatized cell areas in a Greenland Eskimo skeletal sample from the period before the European colonization of Greenland and from different regions of ancient Greenland. As areas of pneumatized cell systems were measured in crania from different parts of Greenland with known significant differences in cranial morphology (Jørgensen 1953; Laughlin and Jørgensen 1956), it was also possible to examine whether the size of the pneumatized cell area was influenced by regional differences in cranial morphology.

V. The fifth study collated the previous four studies and aimed to estimate the frequency of IMED in the three samples, corrected for differences in the pneumatized cell area distribution among the samples. This enabled us to assess the frequency of IMED in Greenland over several centuries.

Background

The pneumatized cell system in the human temporal bone has been the subject of numerous investigations. Between the 1890s and the 1930s studies of the temporal bones were predominantly conducted on cadaver material, but since then most studies have been clinical surveys and animal experiments. Previous studies have shown a significant relationship between small or highly asymmetrical pneumatized cell areas of the temporal bones and infectious middle ear diseases (IMED), i.e. chronic otitis media (COM), recurrent acute otitis media (RAOM) and secretory otitis media (SOM) or chronic tubal dysfunction (CTD) (Bröste 1931; Diamant 1940; Friedmann 1957; Diamant et al. 1958; Palva and Palva 1966; Arora et al. 1978; Sadé and Hadas 1979; Hussl and Welzl-Muller 1980; Hug and Pfaltz 1981; Tos and Stangerup 1984). These findings have been confirmed in animal experiments (Friedmann 1955; Kuijpers et al. 1979; Aoki et al. 1986; Hörmann 1986; Ikarashi et al. 1994).

The temporal bones are almost always abundant and well-preserved in skeletal collections. The structures in the temporal bone seem appropriately protected from postmortal damage. This is due to the morphological and osteological structure of the temporal bone. The most fragile parts of the temporal bone are the tip of the mastoid, the styloid process, the zygomatic process and the middle ear ossicles. When skeletal material is collected, the cranium is usually the most striking object, and crania have often been the only skeletal remains collected, especially in earlier excavations.

These factors favour the study of the palaeopathology of diseases in the temporal bones. Previous systematic studies of middle ear infectious disease are few (Gregg et al. 1965; Rathbun and Mallin 1977; Titche et al. 1981; Gregg and Steele 1982; Bruintjes 1990). Others have published more sporadic reports (Brothwell and Sandison 1967; Cockburn et al. 1975; Schultz 1979; Babin et al. 1990). The techniques used in the studies have included macroscopical examination of the ear region, examination of middle ear ossicles, radiography and CT scanning of the temporal bones. None has involved objective planimetrical measurements of the pneumatized cell areas of the temporal bones. Gregg et al. (1965) studied the pneumatization of the temporal bones of 679 skulls from South Dakota Indian burials, both pre-Columbian and post-Columbian. The temporal bones in the material were analysed radiographically in two projections (Law's lateral projection and Stenver's oblique-posterior-anterior projection). Later, Gregg and Steele (1982) compared this study with studies of 795 adult patients who were born either in the pre-antibacterial drug period or in the antibacterial drug era. In addition, 148 Native American schoolchildren, predominantly of Sioux origin, were examined. The subjects were questioned about any history of OM. Instead of measurements of area, subjective categories were used, based on the morphological appearance of the pneumatized cell system. Gregg and Steele found a higher frequency of normally pneumatized temporal bones in the pre-Columbian period than in the Columbian period. OM was also found to have had a greater effect in the pre-antibacterial era subjects and in the cranial material than in the present-day schoolchildren. The same study design was used by Titche et al. (1981), who studied 742 prehistoric Indians in the period 950-1450 AD, and by Rathbun and Mallin (1977) who studied middle ear disease in 15 prehistoric Iranians from the period 1300-300 BC. Schultz (1979) examined European and Indian anthropological material from 500-1490 AD and used radiography, but only on material macroscopically suspected of ear disease. These studies were therefore biased to various degrees but did indicate that IMED existed in ancient populations. CT scanning of the temporal bones has been used in sporadic studies, especially of Egyptian mummies (Cockburn et al. 1975; Babin et al. 1990).

Outline of the development of the pneumatized cell system

According to Schuknecht and Gulya (1986) and Bast and Anson (1949), the pneumatized space in the temporal bone can be divided into five main regions: the middle ear region, the mastoid region, the perilabyrinthine region, the petrous apex region and the accessory regions (see Fig. 1)

The development of the pneumatized cell system begins in the fourth week of gestation with the formation of the middle ear region (the tympanic cavity and the antrum) and the formation of the Eustachian tube. These structures will not be discussed further in this study. Pneumatization is a hollowing-out process,

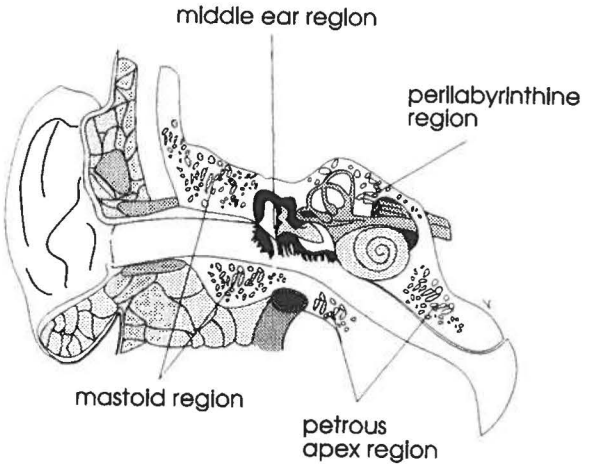

Fig. 1. Oblique view of the temporal bone. The pneumatized regions are shown. The accessory regions are not included.

probably caused by expansion of the mucosa into the foetal mesenchyme and primary bone. This results in communicating air cells which in turn communicate with the middle ear, the antrum and the Eustachian tube. Pneumatization of the petrous and perilabyrinthine regions begins in the 24th week of gestation shortly after ossification of the otic capsule, while pneumatization of the mastoid begins at 33 weeks. At birth, the pneumatized cell system is thus already formed, but still poorly developed. The cell system is enlarged during growth and achieves its final size at the age of 12-14 (Rubensohn 1965). The cell system is lined with a ciliated low cuboidal epithelium which originates from the nasopharyngeal epithelium (Buch 1967; Hentzer 1973). The tympanic cavity is predominantly lined with ciliated columnar epithelium, containing goblet cells which increase in number as they approach the isthmus of the Eustachian tube (Hentzer 1973; Bak-Pedersen 1977).

In certain very rare diseases/disorders such as Franceschetti's syndrome or aplasia of the Eustachian tube, the cell system is poorly developed or totally sclerosed. These inborn diseases/defects are characterized by additional morphological disturbances in the craniofacial skeleton and can therefore quite easily be detected in skeletal material.

Theories of otitis media and the pneumatized cell system

The pneumatized cell system in the temporal bones has been extensively studied since 1879, when Zuckerkandl examined 250 temporal bones (see Bröste 1931; Diamant 1940), but the function and significance of the system are still not physiologically fully understood. Some claim that the system serves as a weight-reducing compartment, others claim that the system serves as a middle ear gas equalizer and others again claim that the system has an immunological function, as it enlarges the mucous membrane surface in the middle ear compartment.

The great individual variability in the size and morphological appearance of the pneumatized cell system has been known since the first macroscopical cadaver studies. This variability was once primarily interpreted as normal biological variation. However, as early as 1904 (Heine) and 1906 (Cheatle) it was recognized that there was a relationship between sclerosed or irregularly pneumatized cell systems and COM (cit. in Turner and Porter 1922; Diamant 1940). Later, radiography supplemented the cadaver studies by permitting examination of living subjects. It was mainly patients with AOM and COM who were studied. In studies of monozygotic twins a high correlation was found between the morphological appearances of the two pneumatized cell systems (Bröste 1931). Anatomical material consisting of 1000 crania was examined for the influence of ethnicity and cranial morphology on the pneumatization of the mastoid process (Turner and Porter 1922). These studies were often taken as evidence of a hereditary or constitutional determination of the pneumatization process. Further research supported the correlation between COM and sclerotic or irregular pneumatized cell systems (Wittmaack 1918; Bröste 1931). This eventually led both to the proposal of the "normal variant" or hereditary theory and to the environmental theory of the pneumatization of the temporal bones, where the whole debate is seen as a "chicken-and-egg" discussion.

Although numerous studies were done, studies prior to the 1940s are in general short on information about the origin of the samples, their age distribution and their exposure to IMED. The studies were to some extent selective and the measurements of the pneumatized cell systems were subjective judgements based on gross anatomy or skiagraphs (X-rays), involving categorizations such as sclerotic, diploic, mixed, atypical and normal pneumatization (Turner and Porter 1922; Bröste 1931). No exact measurements were made. In addition, the techniques used and the pneumatized cell regions that were considered interesting often varied so much that comparisons among the studies are impossible. There are detailed reviews of the literature on the subject before 1940 by Bröste (1931) and Diamant (1940).

The hereditary theory

The hereditary theory of pneumatization holds that sclerotic or hypocellular cell systems occur as an inborn character which predisposes for COM (Diamant 1940). Among the most important studies supporting the hereditary theory are Diamant (1940, 1957), Diamant et al. (1958), Sadé et al. (1979, 1989),

Shatz and Sadé (1990), Shulter-Ellis (1979) and Zaidi (1989).

Diamant (1940) conducted an extensive examination of temporal bone pneumatization and was the first to use planimetrical measurement of the pneumatized cell areas as seen on X-rays. The Runström II lateral projection of the temporal bones was used as the standardized X-ray technique (Runström 1933). Diamant's studies included a study of 320 so-called normal adult subjects who had been hospitalized with scarlet fever, a study of 123 subjects who presented AOM at the time of hospitalization for scarlet fever, a study of 275 subjects with COM from his own practice and a study of 144 people with AOM. Diamant very convincingly demonstrated the close relationship between hypopneumatization and COM. The smallest areas were present in patients with marginal tympanic membrane perforations (mean = 1.81 cm^2), followed, in increasing order of area, by patients with doubtful marginal or central perforations (mean = 2.75 cm^2), patients with central perforations (mean = 4.15 cm^2) and lastly patients with central atrophic scar healings (mean = 6.54 cm^2). In addition, but less convincingly, the patients with AOM had smaller cell areas than subjects in the normal material. The distribution of pneumatized cell areas in the normal subjects was almost normal, with a mean area of 12.71 cm^2 for males and 12.86 cm^2 for females. However, sexual dimorphism was found in children aged 10-15, as girls had larger areas than boys. Diamant ascribed this to hormonal influence on growth. The asymmetry in the material between right and left pneumatized cell areas was explained as normal individual variation, since larger areas were found equally often in the right and left ear. Diamant interpreted the findings as evidence confirming the hereditary theory. There have been objections to this, since Diamant had no information on previous middle ear infections in the normal subjects, and did not conduct otoscopic examinations of the normal subjects (Tumarkin 1959; Tos 1982). It is also questionable whether scarlet fever patients can be considered normal subjects.

In later studies Diamant and co-workers (Diamant 1957; Diamant et al. 1958) examined the pneumatized area distribution in monozygotic and dizygotic twins and in patients with SOM as detected by otomicroscopy. The twin study indicated more hereditary influence than environmental influence. Asymmetry could not be significantly related to heredity. The SOM study showed significantly smaller pneumatized cell areas in ears with SOM than in non-SOM ears. This was interpreted by Diamant to mean that SOM showed a predilection for ears with relatively small pneumatized cell areas.

Other investigators have found frequency variations in the morphological appearance and size of the pneumatized cell systems in different racial populations. Turner and Porter (1922) concluded from a skiagraphic examination of the structural type of the mastoid process in 1000 crania that the frequency of cellular and acellular mastoid processes varies with cranial morphology (low percentages of acellular mastoids in brachycephalic crania) and with race. No sexual dimorphism or correlation with the development of the frontal sinus was found in this respect. No statistical analyses were carried out. In crania from blacks, whites, American Indians and Eskimos Schulter-Ellis (1979) found acellular mastoid processes in frequencies of 40.4%, 34.2%, 31% and 12.4% respectively, and in significantly lower frequencies in female crania. No thorough description of the material was provided. Zaidi (1989) reported lower mean pneumatized areas in brachycephalic Pakistanis than in the dolichocephalic Europeans. It has been claimed that these studies support the hereditary theory. However, none of the studies included information on previous episodes of OM.

Sadé et al. (1979) examined 52 children with different results from treatment for SOM. Group B consisted of 26 children who recovered after one surgical intervention. Group D consisted of 26 children who did not recover after two surgical interventions. Group D had significantly smaller cell areas than group B. No information on OM episodes in early childhood was available. Sadé argued that the study supported the hereditary theory because group B and D were equally associated with SOM. He did not consider the association between the severity of the disease and pneumatization. However, Sadé stated that "the study does not exclude inflammation as an additional factor in the final outcome of the extent of pneumatization". Another study by Sadé et al. (1989), concerning pneumatization in otosclerosis, showed that patients with otosclerosis had significantly larger cell areas than a control group with no history of OM. As patients with otosclerosis are supposed to have had as high a frequency of OM in childhood as a normal population, Sadé suggested that in these patients IMED has had little effect on pneumatization, and that this supports the hereditary theory. Additionally, Shatz and Sadé (1990) found significantly shorter distances between the sigmoid sinus and the external ear canal in COM patients with sclerotic cell systems than in control groups with no history of OM. They thus argued for the hereditary theory, claiming that the position of the sigmoid sinus is established long before birth. However, Sadé and co-workers did not exclude the possibility that postnatal factors may influence the final outcome of the pneumatization process.

The environmental theory

Wittmaack (1918) proposed the environmental theory of temporal bone pneumatization on the basis of microscopic studies of selected human temporal bones

from foetuses and either healthy infants, children and adults or those with middle ear disease. The environmental theory maintains that sclerosed or irregular cell systems are the result of aseptic middle ear inflammation due to the presence of amniotic fluid containing meconium early in infancy or infection of the middle ear later in infancy and childhood. The subsequent change in the constitution of the mucous membrane lining of the pneumatized cell system is considered important, and the resulting sclerosed or irregular pneumatized system is then claimed to be the main determinant of the later development of COM. As Wittmaack did not directly measure the pneumatized cell area, the environmental theory was later expanded to include hypocellularity as an outcome of aseptic middle ear inflammation or IMED in infancy or childhood.

Buch (1967) examined temporal bones from 73 neonates who were either stillborn or had died in infancy. Mesenchyme was present, still unresorbed, in the tympanic cavity to varying degrees. Amniotic fluid or meconium was found in 56 of the children, and 31 of these had inflammatory cells in the tympanic cavity. Inflammation of the stroma was only found in 14 children, all of whom also had amniotic debris in the tympanic cavity. Infiltration with inflammatory cells was not found in any of the children who had mesenchyme throughout the tympanic cavity. This study thus confirmed the influence of external factors in the middle ear which may disturb the pneumatization process. According to Buch, others who had studied somewhat older children had found higher frequencies of leucocyte infiltration, and Buch argued that leucocyte infiltration is fairly rare in immediate infancy but increases shortly afterwards because of the septic environment. The material was highly selective and could not be considered to represent a normal population.

Other claims of the environmental theory are that infection, haemorrhage, obstruction or pressure changes in the middle ear compartment act as primary conditions inhibiting the hollowing-out of the pneumatized cell system in infancy and early childhood. The most important supporters of the environmental theory include Opheim (1944), Ojala (1957), Friedmann (1955, 1957), Tumarkin (1959), Palva and Palva (1966), Arora et al. (1978), Kuijpers et al. (1979), Hug and Pfaltz (1981), Qvarnberg (1982), Tos (1982), Todd (1983), Tos et al. (1984, 1985), Tos and Stangerup (1984, 1985a,b), Stangerup and Tos (1986), Aoki et al. (1986), Hörmann (1986), Rudin et al. (1987) and Ikarashi et al. (1994).

Animal experiments on chickens (Opheim 1944; Ojala 1957), guinea pigs (Friedmann 1955; Hörmann 1986), rats (Kuijpers et al. 1979) and pigs (Aoki et al. 1986; Ikarashi et al. 1994) have demonstrated the effects of exogenous manipulation on the pneumatization process by arresting, inhibiting or temporarily interfering with growth. Opheim (1944) studied the development of the foramen pneumaticum of the chicken humerus, which he claimed resembles the pneumatic development of the human temporal bone. He concluded that the mucosa was of no importance in the development of the pneumatic space in the chicken humerus, but found that certain sufficiently radical exogenous stimuli could interfere with the development. This was in line with the idea that OM in infancy and early childhood may disturb the development of the pneumatized cell system. In a similar study, where the foramen pneumaticum of the chicken was occluded, Ojala (1957) confirmed arrestation of the growth of the pneumatic space in the chicken humerus. However, unlike Opheim, Ojala found evidence that this was due to inflammatory changes in the mucosa. Friedmann (1955) studied experimental OM in full-grown guinea pigs. Bacteria cultured from human OM were unilaterally injected into the middle ear cavity through the tympanic membrane. X-rays showed thickening of the bulla wall on the affected side and the histopathology of the decalcified tissue showed gross thickening of the bulla wall and sometimes complete bony obliteration of the middle ear cavity. Kuijpers et al. (1979) examined the effect of tubal occlusion on the rat middle ear. Prolonged tubal occlusion resulted in marked osteoblastic activity, thickening of the bony surroundings and even obliteration of the rat bulla. In non-decalcified tissue Hörmann (1986) found new bone formation in the lamina propria of the middle ear mucosa in an animal experiment using full-grown guinea pigs. The Eustachian tube was occluded, which resulted in a change in the middle ear pressure as measured by tympanometry. The extent of new bone formation depended on the duration and intensity of the reduced middle ear pressure. This osteoneogenesis was not seen in control animals with normal middle ear pressure. Recently, studies on piglets involving unilateral transtympanic injection of glycerine into the middle ear cavity have shown inhibition of the development of the pneumatized cell system in the experimental ears but normal development in the control ears (Aoki et al., 1986; Ikarashi et al. 1994). However, it has been questioned whether these findings can be applied to the development of the human temporal bone and whether the experimentally-induced conditions resemble human infections of the middle ear cavity.

Histopathological studies in humans with COM (Friedmann 1957; Palva and Palva 1966) have revealed evidence of increased bone resorption (osteoclasts) and remodelling (osteoblasts) leading to obliteration and sclerosing of the pneumatized cells. Friedmann (1957) concluded from his large study of 796 mastoid bone-chips, that "sclerotic as opposed to compact mastoid bone is the effect of chronic infection of the middle ear".

Several clinical studies have been done. In 100 pa-

tients with CSOM, Arora et al. (1978) showed that the pneumatized cell area correlated inversely with the duration of disease.

Hussl and Welzl-Muller (1980), Lindeman and Shea (1980) and Lindeman et al. (1981) found significantly smaller pneumatized cell areas in children with SOM than in healthy children. These two studies were cross-sectional surveys, and neither showed a preference for any of the theories of pneumatization.

Hug and Pfaltz (1981) found significantly smaller cell areas in children with SOM or RAOM than in a control group. By comparing cell areas in groups before and after treatment with either adenoidectomy, adenoidectomy and ventilating tubes or long-term ventilating tubes they found that the increase in area was greater in the long-term ventilating group. The observation period between the first X-ray examination and treatment and the second X-ray examination was 8-12 months. Hug and Pfaltz argued that SOM and RAOM are responsible for the inhibited pneumatization.

Qvarnberg (1982) examined 232 children with AOM and found almost the same age-related area distribution as Rubensohn (1965) did in presumed normal material consisting of Swedish children attending the Ear, Nose and Throat Ward for any reason except middle ear infections. Qvarnberg found that small cell systems and destruction and thickening of the air cell walls were associated with uncured AOM.

Tos and Stangerup (Tos 1982; Tos and Stangerup 1984; Tos et al. 1984; Tos and Stangerup 1985a,b; Tos et al. 1985; Stangerup and Tos 1986) did a series of prospective cohort studies involving neonates, two-year-olds and four-year-olds who were regularly subjected to otological examinations, tympanometry, registration of intermediate episodes of IMED and URIs, and who by the age of six, seven or eight were X-rayed using the Runström II lateral projection. Subsequent planimetrical measurements were carried out in blind trials. Although the number of drop-outs was high, it could be shown that the drop-outs did not appear to differ in their tympanometric scores from the rest of the sample. The studies showed that in a random population of children, the distribution of varying tympanometric scores indicating a range from healthy to severe SOM resembled normal distribution. Tos related this finding to Diamant's normal distribution of pneumatized cell areas and interpreted this as conflicting with the hereditary theory and supporting the environmental theory (Tos 1982). In all three cohorts, too, significantly smaller pneumatized cell areas were found in children with CTD or SOM (high tympanometric score) than in healthy children (low tympanometric score) (Tos and Stangerup 1984; Tos et al. 1984, 1985). Since SOM is related to episodes of URI they proposed the following causative sequence: URI leads to Eustachian tube dysfunction, which in turn leads to SOM and inflammation or infection of the middle ear mucosa, and finally leads to the arresting of the pneumatization process. Significant sexual dimorphism (girls had larger cell areas than boys) was explained by the significantly higher frequency of SOM in the boys (Tos and Stangerup 1985b). Increasing bilateral asymmetry of the pneumatized cell areas was significantly correlated with SOM in terms of the higher tympanometric score on the side with the smaller area (Tos and Stangerup 1985a). Stangerup and Tos (1986) conducted an additional blind prospective study of 33 children with bilateral Type B tympanograms who were treated with adenoidectomy, insertion of a ventilating tube in the right ear and paracentesis in the left ear, and were X-rayed seven years later in the Runström II lateral projection. Significantly higher asymmetry was found in the group with larger areas on the ventilating tube side than in the group with larger areas on the paracentesis side. In addition, significantly larger areas were found on the ventilating tube side than on the paracentesis side in the former group, whereas there was no significant difference in the latter group. Tos and Stangerup concluded from the prospective studies that external factors like inflammation and infection affect the otherwise genetically determined growth of the pneumatized cell system, and that this supported the environmental theory.

In a population study of different cohorts in Sweden, Rudin et al. (1987) found that the pneumatized area correlated positively with cohorts from the higher social classes, of greater height and younger age. Area was correlated with the extent of tympanic membrane pathology and positive OM history in childhood and adolescence, but not in adulthood. Rudin concluded, like Tos and Stangerup, that the pneumatized area is to some extent genetically determined, but is also influenced by environmental factors.

Dietzel (1989) found no normal distribution of pneumatized cell areas in a sample consisting of 315 patients with skull traumas. However, the same objections to the normality of the material can be made to Dietzel's study as to Diamant's study.

Implications for the present study

The number of studies in the literature favouring the environmental theory greatly exceeds the number favouring the hereditary theory, and the tendency in the more recent studies is to say that genetic as well as environmental factors are important to the final outcome of pneumatization. The only prospective study done also supports the environmental theory, as do all the animal experiments. Supporters of the hereditary and the environmental theory both acknowledge that hypocellular or highly asymmetrical pneumatized cell systems are closely related to episodes of IMED in childhood, irrespective of causal relationship. This

study takes advantage of the agreement on this point by assuming that hypocellular or highly asymmetrical pneumatized cell areas represent ears where episodes of IMED have occurred in childhood. However, the present study design does not permit exploration of any of the theories.

Otitis media in Greenland Eskimos

According to Meldorf (1907) the first report of possible OM in Greenland is from 1752. Cranz, a German missionary, observed a disease in the Eskimos that caused severe headache, chest pain and violent earache. The first district physician in Greenland, F. Bloch, who was sent out to practice in South West Greenland in 1839, reported after one year that URIs and earache were both very common. Ibsen reported from Godthåb (now Nuuk) in 1881 and 1883 that OM was a frequent complication in flu epidemics. In 1889 the district physician Kiœr reported from North West Greenland on frequent Eustachian tube disease and OM which often remained active longer than the acute stage. This was confirmed by Lindemann in Julianehåb in 1891. Meldorf stated in his own report from Julianehåb district in 1899 that COM with ear discharge was very common, especially among the children, and was probably caused by the frequent URIs in Greenlanders, which are transmitted to the middle ear along the Eustachian tube. The district physician Alfred Bertelsen confirmed Meldorf's observations in his thesis from 1940 and mentioned that OM was almost a constant symptom among the children (Bertelsen 1940). Bertelsen ascribed these findings to anatomical characteristics of the Eskimos.

Since the 1950s otologists from Denmark have regularly visited Greenland and have with remarkable consistency reported high frequencies of middle ear infections.

The first epidemiological survey of OM in Greenland was done by Pedersen and Zachau-Christiansen (1986, 1988) in short periods of the summers of 1983 and 1984. The study took place in the towns of Ilulissat (Jakobshavn) and Maniitsoq (Sukkertoppen) and in the village of Kangamiut near Maniitsoq. The test sample was randomly chosen from the Danish National Population System and the examinations included otomicroscopy and tympanometry. The survey included 142 children aged 3-8 and 608 sub-adults and adults aged 11-20 and 41-50. The results of the study confirmed the high prevalence of OM in Greenland, especially among children. Lately, this has been further demonstrated in a survey of 591 children in the same age groups in Nuuk and Sisimiut, Greenland (Homøe et al. 1996).

Table 1. The three study materials and the sex distribution.

Study materials	N	Male	Female
Modern living Greenlanders	34	16	18
Historical Eskimos	56	24	32
Prehistorical Eskimos	127	54	73

Samples and Subjects

The study material consists of two skeletal samples from Greenland Eskimos, one historical and one prehistoric, and a sample from modern living Greenlanders (see Table 1). The skeletal samples are part of the Greenlandic collections at the Laboratory of Biological Anthropology, University of Copenhagen. The Greenlandic collections comprise skeletal remains of approximately 1500 individuals. Only part of the material in the collections has been archaeologically dated and some of the material is deficient with respect to almost all archaeological details. Given the purpose of the study, thorough scrutiny and selection of the material is crucial. The Greenlandic material is registered in a database and the samples of crania were retrieved from this database (Lynnerup et al. 1992a). The interesting crania were then examined for their state of preservation and were chosen if this was acceptable. Items considered important were well preserved mastoid processes and crania in a condition which permitted accurate cranial measurements to be obtained.

The typical Greenland Eskimo cranium is large and dolichocephalic. The nose is high and very narrow with small nasal bones. The orbitae are large and high. The zygomatic arches are broad and protruding, and the lower jaw (mandible) is broad. In general the muscle insertions are fairly powerful. The tooth wear is pronounced, especially in female crania (Jørgensen 1953).

Pilot study

The sample used in the pilot study comprised 56 historical Eskimo crania (32 females, 24 males) (Homøe and Lynnerup 1991) (from now on called "historical Eskimos"). The material came from the Uummannaq district on the west coast of Greenland (see Fig. 2) and was chosen for the pilot project because of its geographical consistency.

Only complete adult crania were included. Of the 106 individuals in the series, 50 crania were excluded as they came from sub-adults, were incomplete, or had too much mummified soft tissue attached, making measurements unreliable.

Anthropological and archaeological considerations

The selected crania were collected by A. Bertelsen, district physician in 1902-27. The skeletal remains are believed to range in age from about the eighteenth

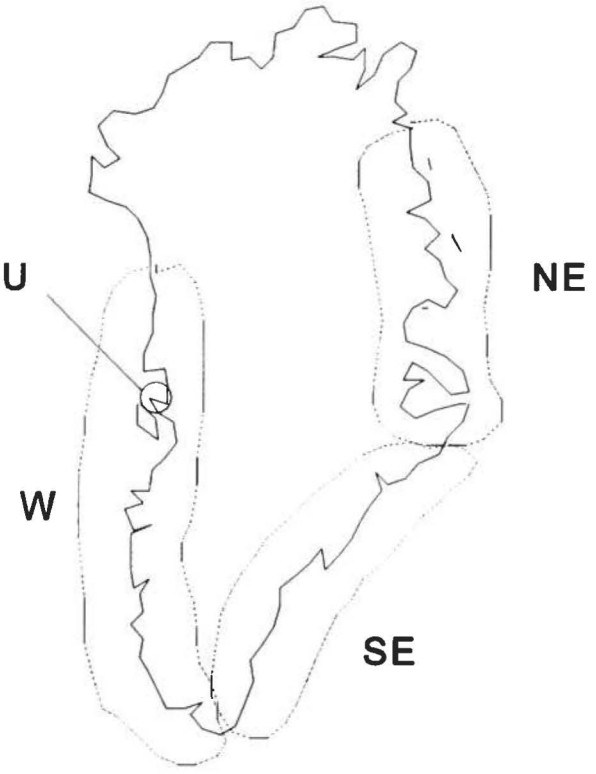

Fig. 2. Map of Greenland. The provenance of the materials are marked. The historical Eskimos came from Uummannaq district (U). The prehistorical Eskimos came from the West Coast (W), the South-East Coast (SE) and the North-East Coast (NE).

to the nineteenth century AD (Frøhlich 1979), but exact dating is not available as the material was not archaeologically excavated. The sample was received by the Laboratory of Anthropology in 1906 and 1923. According to Frøhlich, the genetic heterogeneity of this material is uncertain but genetic influence from Europeans is believed to have been of minor importance. However, cultural influence is believed to have been significant, for example since smallpox epidemics in the Inuit population were reported in this period (Meldorf 1907; Gad 1969; Frøhlich 1979).

Modern Greenlanders

The living subjects, from now on called "the modern Greenlanders", were primarily studied in 1976-77. The material comprises X-rays of temporal bones and questionnaires on prior IMED in childhood answered by thirty-six Greenlanders born in Greenland (Homøe et al. 1994). Originally, this material was sampled for a study of the normal pneumatized cell area in Greenlanders compared with Danes. However, this study was never published. The individuals were randomly selected from Greenlanders admitted to various wards at Rigshospitalet, the University Hospital in Copenhagen, which is the referral hospital for Greenland. All participated in the study after giving their informed consent.

Of the initial 36 subjects in the study, two were excluded because of inconclusive questionnaires: this left 34 subjects in the study, 18 of whom were females and 16 males, with an age span from 14 to 65 (median = 37.5 yrs., interquartile range = 27 – 47 yrs.). The subjects came from all parts of Greenland.

Table 2. Description of the origin of the prehistoric Eskimo material

Archaeologist	Excav. year	N	Male/Female	Excavation site
Ryder	1891-92	4		Føhnfjord, Nordvestfjord
Thostrup, Brønlund	1908	2		Dovebugt, Kap Beurmann Nœs
A. Petersen	1924-25	4		Kap Hope, Kap Tobin, Scoresbysund
P.V. Glob, L. Koch	1932-33	5		Clavering Ø, Suessland
H. Larsen, L. Koch	1932, 35, 37	10		Clavering Ø, Nordfjord, Scoresbyland
Single finds	?	4		NE, Sabine Ø, Kap Mary, Andreeland
North-East* (NE)	1891-1934	29	13/16	
G. Holm	1883-85	10		Ammassalik, Dronning Louise Ø, Kuutseq, Anoritsoq
G. Amdrup, K. Poulsen	1898-99	9		Saqqarmiut, Ammassalik
H. Larsen	1935	1		Kangerlussuaq
T. Mathiassen	1932	22		Avaqqat, Nørre Skjoldungen, Timmiarmiut Ammassalik Fjord, Sermilik
South-East* (SE)	1883-1935	42	20/22	
T. Mathiassen	1929	12		Upernavik, Inugsuk, Gl. Skibshavn
T. Mathiassen	1930	4		Kangamiut, Narsarmiut
T. Mathiassen	1933	16		Qeqertaq, Igllorsuit, Illutalik
T. Mathiassen	1934	22		Tugtutoq, Uummannalik, Unnartoq Fjord, Narsarsuaq
J. Meldgård	?	2		Qornoq, Sarfat nearby Nuuk
West* (W)	1929-1934	56	21/35	

*NE: from Scoresbysund and north
*SE: from Kap Ummarnarsuaq (Kap Farvel) – Kap Ravn (south of Scoresbysund)
*W: from Kap Ummarnarsuaq (Kap Farvel) – Upernavik

The use of the material in this study was approved by the Copenhagen Ethics Committee Case No. (KF) V 92-021, in accordance with the Helsinki II Declaration.

Prehistoric Greenland Eskimos

This sample, from now on called "prehistoric Eskimos", consisted of 127 adult Eskimo crania (54 males, 73 females) excavated at different locations and different periods in Greenland (see Table 2) (Homøe et al. 1995). Fifty-six were from the west coast (W) of Greenland, 42 were from the south east coast (SE) and 29 were from the north east coast (NE) (see Fig. 2). Only adult, almost complete crania presenting two well preserved temporal bones were included in the study.

Anthropological and archaeological considerations

All the crania included had been determined archaeologically to be from the pre-European colonization period of Greenland (west coast, before 1721 AD; east coast, before 1884 AD) (Holm and Garde 1889; Ryder 1895; Amdrup 1909; Mathiassen 1930, 1931, 1933, 1934a,b, 1936a,b; Larsen 1934; Glob 1935; Jørgensen 1953). The material was arranged by excavation region into W, SE and NE in accordance with the theory of the migrations of the Eskimos in Greenland (Jørgensen 1953; Laughlin and Jørgensen 1956; Koch 1989). Although there had been contact between the Eskimos and the Europeans, including the Norsemen, on the west coast before 1721, the encounters were presumably only occasional and for commercial purposes (Gad 1967; Frøhlich 1979). This sample is thus considered to be without European genetic or cultural influence.

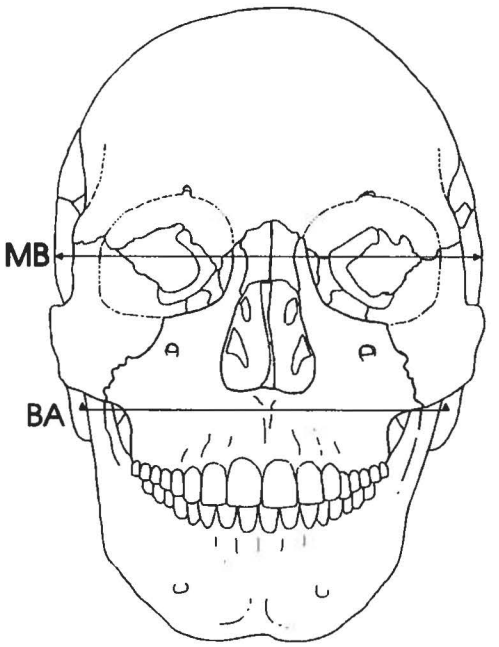

Fig. 3. Frontal view of a cranium. MB = maximal breadth, BA = biauricular breadth.

Methods and validation procedures

This section describes the methods used in the study, discusses the possible errors and bias inherent in the techniques, and states the procedures used to minimize the errors and bias.

Determination of sex and age

Although part of the prehistoric Eskimo sample has previously been studied anthropologically (Jørgensen 1953), all crania included in this study were assessed for sex and age to ensure homogeneous results permitting comparison of the two skeletal samples. Sex and age were determined in accordance with standard anthropological procedures (Workshop of European Anthropologists 1980). Sex determination was based on the size of the crania; the size of muscle insertions, especially those of the superior orbit and the occiput; the size of the mastoid process; and the extent of dentitional wear. According to other sources, sex in skeletal samples can usually be determined with an accuracy of 90%-95% (Workshop of European Anthropologists 1980; Lynnerup 1995). As sex was determined in this study solely from the crania, the accuracy is likely to be less – the accuracy of such determinations has previously been estimated as 85% (Workshop of European Anthropologists 1980). Age was determined by examining teeth and cranial sutures, and was meant solely to distinguish between adults and non-adults.

Anthropometrical measurements

Anthropometrical measurements were made to establish any possible correlation between the pneumatized area and craniofacial morphology. Each cranium was measured using digital calipers with an accuracy of 0.05 mm.

In the pilot study the craniofacial variables measured were maximum length (M1), basion-nasion length (M5), maximum breadth (M8), biauricular breadth (M11), basion-bregma height (M17), basion-prosthion length (M40) and nasion-prosthion height (M48), all according to the standardized procedures described by Martin (Martin 1988) (see Figs. 3 and 4).

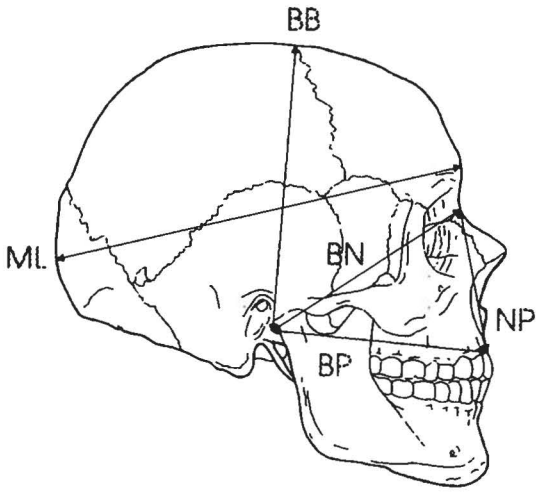

Fig. 4. Lateral view of a cranium. ML = maximal length, BB = basion-bregma height, BN = Basion-nasion length, BP = basion-prosthion length, NP = nasion-prosthion height.

In the study of the prehistoric Eskimo sample, the anthropometrical variables measured were maximum length (M1), basion-nasion length (M5), maximum breadth (M8) and basion-bregma height (M17), all according to Martin (see Figs. 3 and 4). These variables were chosen in order to describe the neurocranium, which was already known to vary among the W, SE and NE samples (Jørgensen 1953; Laughlin and Jørgensen 1956). In this sample the maximum breadth could not be obtained in one cranium and the basion-nasion distance could not be obtained in two crania because of postmortal damage.

No craniofacial measurements were made of the modern Greenlanders.

Radiography

The X-ray projection chosen for the study was the Runström II lateral projection, also known as Runström's B-ear projection (Runström 1933). This was chosen because it has been used in most of the clinical studies of the pneumatized cell area and thus provides a basis of comparison among the studies (Diamant 1940; Diamant et al. 1958; Flisberg and Zsigmond 1965; Lindeman and Shea 1980; Lindeman et al. 1981; Tos and Stangerup 1984; Rudin et al. 1987). Other projections are available, and in a study by Todd et al. (1987) of 30 cadaver specimens these projections were found to give comparable and highly correlated measurements. In addition, Todd et al. found correlation coefficients between 0.57 and 0.74 of the pneumatized volumes calculated from CT scans and the areas measured with the various X-ray techniques. Other studies (Flisberg and Zsigmond 1965; Andréasson 1976) have also shown correlation between measured volume and area in clinical material. In Flisberg's gas-volumetric study, correlation coefficients were as high as 0.75 – 0.90 in the various clinical samples consisting of subjects with healthy ears and those with COM.

The crania were mounted in the Frankfurt plane (a horizontal line through the border of the inferior orbit and the external ear canal) on a Siemens ORBIX table and the X-rays were taken with a film-focus distance of 125.50 cm, a film-object distance of 8.00 cm and at a 10° angle in the frontal plane (see Fig. 5). The magnification factor was 6.8%, calculated as the object-film distance divided by the focus-object distance. The X-ray films were Kodak T-Mat G-film 5500 in boxes with Kodak Lanex Regular amplification foils. The exposure was made at 60 Kv and 2.5-4.0 Mas.

All X-rays of the crania were taken at the Department of Radiology, Royal Dental College, Panum Institute. In order to standardize the technique and minimize the possibility of error, all X-rays were taken with the same X-ray apparatus and by the same radiologist. The X-rays were coded so that subsequent measurement of the areas could be done in blind trials.

Each of the modern Greenlanders was also X-rayed in the Runström II projection. This was done at the Department of Radiology, Rigshospitalet, with another X-ray apparatus. The film-focus and film-object distances were 90 cm and approximately 3 cm respectively. The magnification factor was 3.5%.

The technical differences between the studies were minor differences in the magnification factor (3.3%) and a 10° angling in the frontal plane in the skeletal material. As this angling caused a slight reduction of the pneumatized cell area due to the slanting, the angling tended to neutralize the difference in the magnification factor. Thus the present study was unique, as X-rays of living subjects and anthropological skeletal material provided results that permitted comparisons of pneumatization.

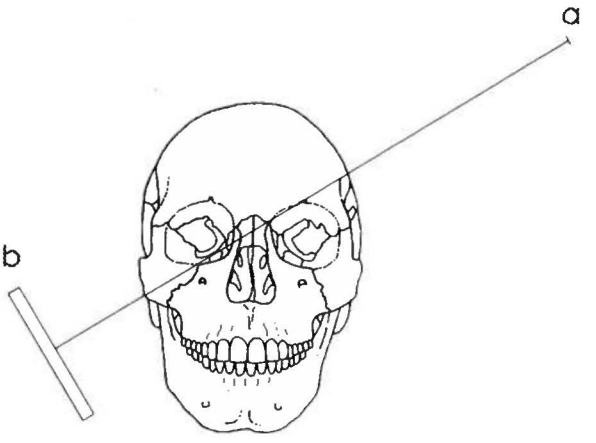

Fig. 5. Illustration of the X-ray technique. The cranium is mounted in the Frankfurt plane. a = focus, b = film.

Possible errors in the X-ray procedure were individual inconsistencies in the distances, angles and slanting of the X-ray apparatus and in the positioning of the crania and the living subjects. Attempts were made to minimize these inconsistencies in the cranial material, as mentioned above. In the prehistoric Eskimo sample two crania had to be X-rayed twice because of an obviously incorrect angle.

Measurement of the pneumatized cell area in the temporal bones

The pneumatized area was measured planimetrically using a computer. The coded X-rays were placed on a translucent digitizer (HiPad, Houston Instruments), mounted on a backlight to enhance the details of the X-rays. The pneumatized area was delineated on a transparency and scanned with the digitizer, which was connected to a standard IBM AT desktop computer. The area was then calculated directly by a BASIC computer program developed for the purpose (Lynnerup et al. 1992b). The program was tested for accuracy prior to the investigations. As in previous studies, the antrum, epitympanon and cavum tympani were not included in the pneumatized cell area (Diamant 1940; Lindeman and Shea 1980; Tos and Stangerup 1984) (see Figs. 6 and 7). This was done to permit comparisons among the studies.

In the prehistoric Eskimo sample the delineation of the pneumatized cell areas were problematical in three cases because of difficulties in distinguishing the superior border of the pneumatized cell system from the spongiosa of the temporal bone. Repeated X-rays of these three crania were therefore taken at a higher voltage.

Accuracy and observer tests of the digitized planimetrical measurement

The pilot study comprised tests for accuracy of the digitizer and the computer program. This was done by repeatedly tracing squares on preformed square paper. As this procedure showed consistent results, the accuracy of the digitizer and computer program was assessed by reading off a delineated area ten times.

Interobserver variation in the delineation and subsequent area calculation was assessed by two observers who independently delineated and read all 112 X-rays.

Both observers also delineated and read twenty X-rays twice at intervals and in different orders to assess the intraobserver variation. The time intervals were chosen to minimize the risk of recall.

Validation with CT scanning

The crania which were considered to have had IMED in the pilot study were CT-scanned at the Department of Radiology, Hvidovre Hospital according to the routine for patients with suspected pathology in the temporal bone – i.c. 2 mm consecutive scan slices, a gantry tilt of 25 degrees from the Frankfurt plane approximately parallel to the axis of the cochlea, and a scanning range from the inferior tip of the mastoid process to well above the middle ear (Homøe et al. 1992). All CT scans were done on the same apparatus (Siemens, Somatron DRG). The CT scanning was done in order to examine the morphology of the pneumatized cell system. The findings expected were sclerosing, obliteration and irregularity of the cell

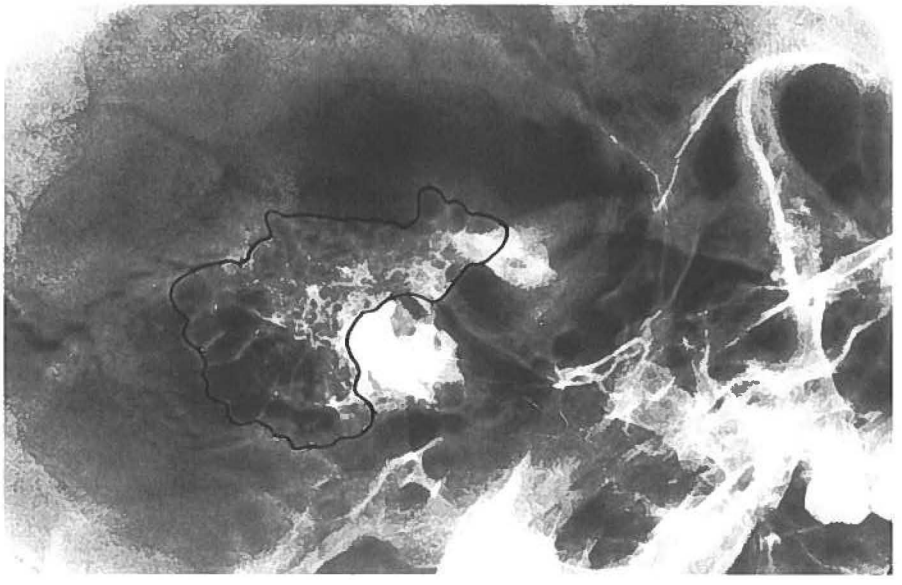

Fig. 6. X-ray of the left side temporal bone in a cranium. The pneumatized cell system is outlined. The area size is normal.

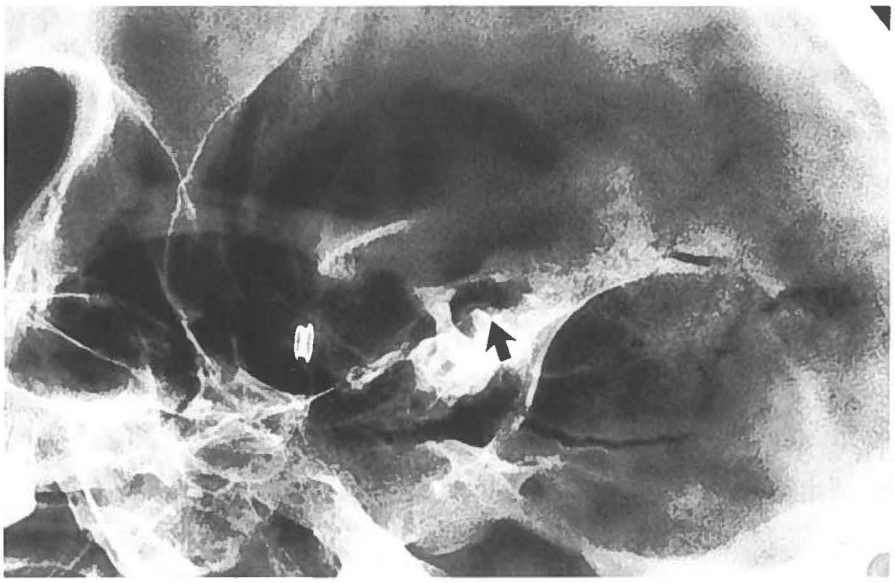

Fig. 7. X-ray of the right side of a cranium. The pneumatized cell system is not visible. Only the middle ear cavity and the antrum mastoideum are aerated (indicated by the arrow).

systems. These morphological characteristics are present in the temporal bones of subjects with COM (Friedman 1957; Palva and Palva 1966). If the crania revealed these characteristics, this was interpreted as supporting the supposition of IMED in the crania on the basis of the pneumatized cell areas.

Questionnaire

The modern Greenlanders were asked, with the help of an interpreter, to complete a questionnaire on previous and/or current episodes of IMED, previous middle ear operations and hearing loss. If the answers indicated IMED, more detailed questions were asked. The classification "IMED in childhood" was based on this and on medical records. We attempted to validate the answers by consulting the medical records in Greenland. Unfortunately, we could not do so, because some records could not be traced or were incomplete, probably as a result of the frequent migration in Greenland.

Particularly important in this study was the issue of IMED in childhood, since this served as a touchstone. Remembering IMED in childhood may be difficult, but this was considered to be of minor importance in this study, since only the more severe diseases such as COM, CTD and RAOM are associated with small pneumatized cell areas. A prospective design would have been preferable, but was not considered feasible in the present context.

Otological examinations

All crania were examined by gross inspection and conventional otoscopy of the external ear canal and middle ear cavity. The crania asserted to have had IMED in the pilot study were in addition examined by otomicroscopy using a standard otomicroscope. These examinations were done in order to look for ante-mortal erosion and destruction of the ear, and other signs of pathology such as malformations or congenital syndromes, especially morphological abnormalities in the cranial vault, the facial skeleton, the mandible, the temporo-mandibular joint and the dentition. In addition, we attempted to measure the size of the bony part of the Eustachian tube using bougie in the prehistoric Greenlanders. The purpose of this was to examine the relationship between the size of the bony Eustachian tube and the pneumatized cell area. In previous studies these have been found to be inversely correlated (Todd 1983). However, we were unable to do this because of the fragile condition of the bony wall.

The modern Greenlanders were all otoscopically examined for pathology of the eardrum, using conventional and pneumatic otoscopy to estimate the severity of the disease. As it is well known that IMED can heal without leaving pathological signs in the tympanic membrane and that pathological signs in the tympanic membrane can heal, this is not adequate as a validation procedure (Tos 1982).

Statistical methods

To obtain a thorough description of the data in the study, we chose to give the median, range and binomial confidence interval and the mean, standard deviation and confidence interval (CI) for the continuous data. In the analysis of the various samples, it was necessary to make a choice between the parametric

and the non-parametric approach. The merit of non-parametric analyses is that one avoids the normal distribution assumption; the disadvantage is less efficient analyses and a strong focus on testing. Since the present study focused more on estimation than testing, and since inspection of the distribution in several situations did not show typical deviations from normality, we decided to rely on normal distribution theory in these situations.

In the testing of hypotheses, a p-value of 0.05 or less was considered significant.

Statistics for accuracy, interobserver and intraobserver variation and biological variation

The accuracy of the digitizing process and computer area calculation was expressed as a coefficient of variation (SD/mean x 100 %). A Mann-Whitney test was initially done on the observer data and indicated no bias between the observers. Similarly, there was no difference between the first and second measurement for each of the two observers. However, non-parametric statistics were not an adequate approach as the variations in the data sets could not be calculated. The latter could be done by using a t-test, which however required acceptance of the normal distribution theory. A t-test could describe the different types of variation singly, but an approach that could describe the variations as a whole was preferred. Within the framework of a variance component model, it is possible to separate the total variation observed in the measurements out into components corresponding to biological (true) variation, inter-observer variation (variation between observers), intra-observer variation (variation in an individual observer) and technical variation. The computations were done with PROC MIXED in the SAS software package.

With subscripts defined as c : crania, o : observer, j = square tracing number and b = delineation number, an individual measurement can be decomposed as:

$$Y_{cobj} = \mu + A_c + B_{co} + C_{cob} + \varepsilon_{cobj}$$

where Y_{cobj} denotes the total variation, μ denotes the grand mean, A_c denotes the deviation from the grand mean for the c'th cranium (the variance of this component is the biological variation), B_{co} denotes the specific contribution from the combination of observer o, cranium c (the variance of this is the inter-observer variation), C_{cob} denotes fluctuations in subsequent evaluations by the same observer (the variance of this is the intra-observer variation); and finally ε_{cobj}, which denotes the deviation due to the technical preparation (the variance of which is the technical variation).

The variance component model permits estimation of all these components separately – in particular the reliability coefficient, which is defined as the proportion of observed variance that can be attributed to the biological material in itself (the true = the biological variation). One source of variation was not separated out by this procedure, namely the variation which comes from a possible deviation in mounting and X-raying the crania. The biological variation therefore includes this. However, as mentioned on pages 13 and 14, this variation is considered to be small.

Additionally, the inter- and intraobserver data were examined graphically as lines of equality and as the differences against the averages with limits of agreement (Bland and Altmann 1986).

Non-parametric statistics for examination of differences in categorial data

Fischer's exact test and the Chi-square test were used to test for differences in frequencies. The binomial distribution was used to give the confidence limits when relevant.

Non-parametric statistics for the examination of differences in continuous data

The Mann-Whitney and Kruskall-Wallis tests were used to test for differences in unpaired data. These tests rank data and are thus on the side of caution, but at the same time the tests reduce the information content of the data (Altmann 1991). Parametric tests were only implemented when statistical significance was obtained in the non-parametric tests. A one-way ANOVA test as implemented by the Systat MGLH ANOVA module was used to examine differences in groups of continuous data (Wilkinson 1990). No formal test for variance homogeneity was carried out; instead, the distributions were studied graphically as in Altmann (1991).

Statistics for correlation and regression analyses

To test for relationships between two continuous variables, Spearman's non-parametric correlation coefficients were used. In order to investigate the influence of cranial variables on area, we used a multiple regression analysis as implemented by the MGLH module of the SYSTAT computer software (Wilkinson 1990). The model was controlled by studying the residuals (Kronborg and Skovgaard 1990; Altmann 1991).

Statistics for estimation procedures and the problem of interdependence

The two ears of each individual are paired with respect to development, growth and risk of disease. As the pneumatized cell areas in the two ears of each individual contribute information, it was relevant to use the polychotomous logistic regression model (Rosner 1984; Homøe et al. 1994).

The polychotomous logistic regression model is an extension of the logistic regression model used to bivariate binary data (Rosner 1984). The model was developed in a study of the eyes but is equally well suited for analysis of the material in the present study, in which ears occur in pairs.

In the present study each patient (or cranium) may have had IMED on both sides (++), on either the right (+−) or the left side (−+) or not at all (−−). Four subgroups can therefore be defined. Following Rosner, intra-individual correlation is modelled by specifying that the probability of having any one ear affected (for an individual with symmetric areas) is Beta-distributed over the population. This leads to a Beta-binomial model for the four subgroups given above. Furthermore, it can be specified that log odds for each subgroup depend on two covariates relating to the areas, i.e. the area on the IMED side and (in unilateral cases) the degree of asymmetry. This means that the model must allow for an "individual effect" and makes it possible to include the information on unilateral IMED carried by asymmetrical areas. For example, if an individual with identical normal areas on both sides is compared with an individual with the same area on the left side but with an area half as large on the right side, it is likely that the latter individual has had IMED in the right ear. The model thus specifies four probabilities (polychotomous) for each individual, according to the four subgroups (++,−+,+−,−−) given by:

$$P(+^{(R)}+^{(L)}) = \frac{\exp(\alpha_2+\gamma_2(A^{(R)}+A^{(L)}))}{Q}$$

$$P(+^{(R)}-^{(L)}) = \frac{\exp(\alpha_1+\gamma_1(A^{(L)}-A^{(R)})+\gamma_2 A^{(R)})}{Q}$$

$$P(-^{(R)}+^{(L)}) = \frac{\exp(\alpha_1+\gamma_1(A^{(R)}-A^{(L)})+\gamma_2 A^{(L)})}{Q}$$

$$P(-^{(R)}-^{(L)}) = \frac{1}{Q}$$

Here, $A^{(L)}$ and $A^{(R)}$ denote the area on the left and right side respectively, and Q denotes the sum of the four numerators, since the probabilities must add up to one.

The parameters α_1 and α_2 originate from the Beta-distribution over individuals describing the individual susceptibilities to ear infections, whereas γ_1 denotes the effect of asymmetry and γ_2 denotes the effect of area as such.

The model was analysed in SAS, PROC CATMOD, using a user-generated design matrix consisting of a 3*4 matrix for each individual.

$$\begin{pmatrix} 0 & 1 & 0 & A^{(R)}+A^{(L)} \\ 1 & 0 & A^{(R)}-A^{(L)} & A^{(L)} \\ 1 & 0 & A^{(L)}-A^{(R)} & A^{(R)} \end{pmatrix}$$

Each row specifies the log odds for a disease group (++,+−,−+) in relation to normal individuals (−−) as a function of the parameter vector $\theta = (\alpha_1, \alpha_2, \gamma_1, \gamma_2)'$. For the modern Greenlanders, the total design is thus of the dimension (34*3)*4, since the total is 34 individuals. On the basis of actual observations of IMED, these probabilities can be estimated for any combination of areas. Given that the present group of individuals is representative of Greenlanders, the classification can be done by allocating an individual to the group with the highest estimated probability. If we consider the results of the questionnaire to be the true IMED distribution, the diagnostic accuracy of the model can be tested by calculating its sensitivity, specificity and positive predictive value. The occurrence of IMED can also be considered as a Bernouilli-distributed variable (0-1 variable) with an estimated probability that is the sum of the three group probabilities (++,+−,−+). This distribution is however more susceptible to error in area measurement than the Beta-binomial distribution, and may therefore tend to overestimate the IMED frequency.

The model was subsequently applied to the skeletal material. Since the model was developed for the modern Greenlanders with a somewhat different area scale than in the skeletal samples, the data for each of the three samples were converted into Z-scores (i.e. areas – mean area divided by the standard deviation of the areas) before the model was applied. This conversion was derived from the bilateral mean value of non-IMED modern Greenlanders and from the non-IMED-classified crania after the first iteration, in which the crania classified as having had IMED were excluded in each of the skeletal samples. The Z-scores denote the distance from the mean of the samples in units of standard deviation and provide a value permitting comparison of the samples that is independent of systematic differences among the samples. As extreme values may have a strong influence on the classification limits, sensitivity was investigated by successively eliminating data with extreme values. The classification limits were found to be almost independent of single values and sample size.

Results and Discussions

This part of the thesis presents the results of the studies in the sequence in which they were conducted. Each section is followed by a discussion. This form was selected to provide a better overview of the studies.

Historical Eskimos

The variation coefficient of the digitizing procedure was 0.06%. No systematic difference in area measurements between the two observers could be detected when non-parametric analysis was used ($p = 0.86$); the mean difference was 151.66 mm^2. Nor was re-measurement of the area found to have any systematic effect for any of the two observers ($p = 0.18$ and $p = 0.48$, respectively); the mean differences were 71.35 mm^2 and 60.00 mm^2. The parametric variance component model estimated the technical variation to be 5.70 mm^2 of the pneumatized cell areas; the intra-observer variation for the two observers was 66.86 mm^2 and 58.76 mm^2 respectively, and the mean for the two observers was 62.94 mm^2. Lines of equality were excellent for each of the observers and the distributions of differences against averages were acceptable (see Fig. 8). The interobserver variation was 145.13 mm^2 and the line of equality was excellent, as was the distribution of differences against averages (see Fig. 8). A t-test for systematic bias between the observers was not significant ($p = 0.89$). The biological variation was estimated to be 438.52 mm^2. The reliability coefficient was calculated as 0.88.

An estimated 12% of the variation in the area thus came from errors in the measurement procedure, while 88% of the variation in area came from the biological variation in the material.

Since all pneumatized cell areas of the historical Eskimo crania were measured by two observers, the areas in this study were calculated as an average of the two observers' measurements. The mean, standard deviation, median and range of the right and left pneumatized cell areas of the 56 crania are shown in Table 3.

Table 3. Descriptive statistics of the right and left side pneumatized cell areas in the 56 historical Eskimo crania. All values in mm^2.

Area size	Mean	SD	Median	Max.	Min.
Left	1495.12	453.06	1607.00	2038.50	51.00
Right	1439.87	454.49	1466.75	2270.00	92.50

The pneumatized cell areas of the 56 individuals were distributed as shown in Figs. 9 and 10. The measured area on each side did not show sexual dimorphism (right side: $z' = 0.414$, $p = 0.68$; left side: $z' = -0.712$, $p = 0.48$).

The difference between the pneumatized areas of the two sides was calculated. The median difference of this asymmetry was 201.50 mm^2, with the 90-percentile = 815.70 mm^2 (mean = 319.14 mm^2, SD = +384.21 mm^2, mean + 2SD = 1087.56 mm^2), Five crania were arbitrarily defined as highly asymmetrical, following the histogram (see Fig. 11), where five crania are clearly isolated from the rest of the sample.

The pneumatized area showed significant bilateral correlation; $r(S) = 0.608$, $p < 0.00001$, (see Fig. 12).

The cranial measurements, along with the cranial index (maximum breadth/maximum length x 100), are shown with their means, standard deviations, medians and ranges for each sex in Table 4 and Table 5.

Correlation coefficients between area measurement on the one hand and each of the various cranial measurements on the other hand were calculated, and only

Table 4. Descriptive statistics of male cranial measurements. N = 24. Values in mm.

Variables	Mean	SD	Median	Max.	Min.
M1 Maximal length	189.90	5.01	189.50	198.00	180.00
M8 Maximal breadth	138.27	4.96	136.75	150.00	131.00
M5 Basion-Nasion	106.23	4.84	106.00	117.00	96.00
M11 Biauricular breadth	113.25	3.86	113.00	123.00	108.00
M17 Basion-Bregma	138.71	4.56	138.00	147.00	132.00
M40 Basion-Prosthion	104.19	4.97	104.75	115.00	94.50
M48 Nasion-Prosthion	73.50	3.12	74.00	79.50	67.00
Index M8/M1 (%)	72.87	3.46	72.29	83.33	67.88

Table 5. Descriptive statistics of female cranial measurements. N = 32. Values in mm.

Variables	Mean	SD	Median	Max.	Min.
M1 Maximal length	181.69	5.66	181.00	198.00	167.00
M8 Maximal breadth	131.94	3.72	131.50	142.00	127.00
M5 Basion-Nasion	101.09	3.71	101.00	108.00	94.00
M11 Biauricular breadth	106.69	4.03	105.50	116.00	98.00
M17 Basion-Bregma	132.64	4.72	132.00	141.00	124.00
M40 Basion-Prosthion	99.50	4.59	100.00	108.50	89.00
M48 Nasion-Prosthion	67.81	4.50	67.50	77.00	61.00
Index M8/M1 (%)	72.67	2.63	72.55	79.64	68.09

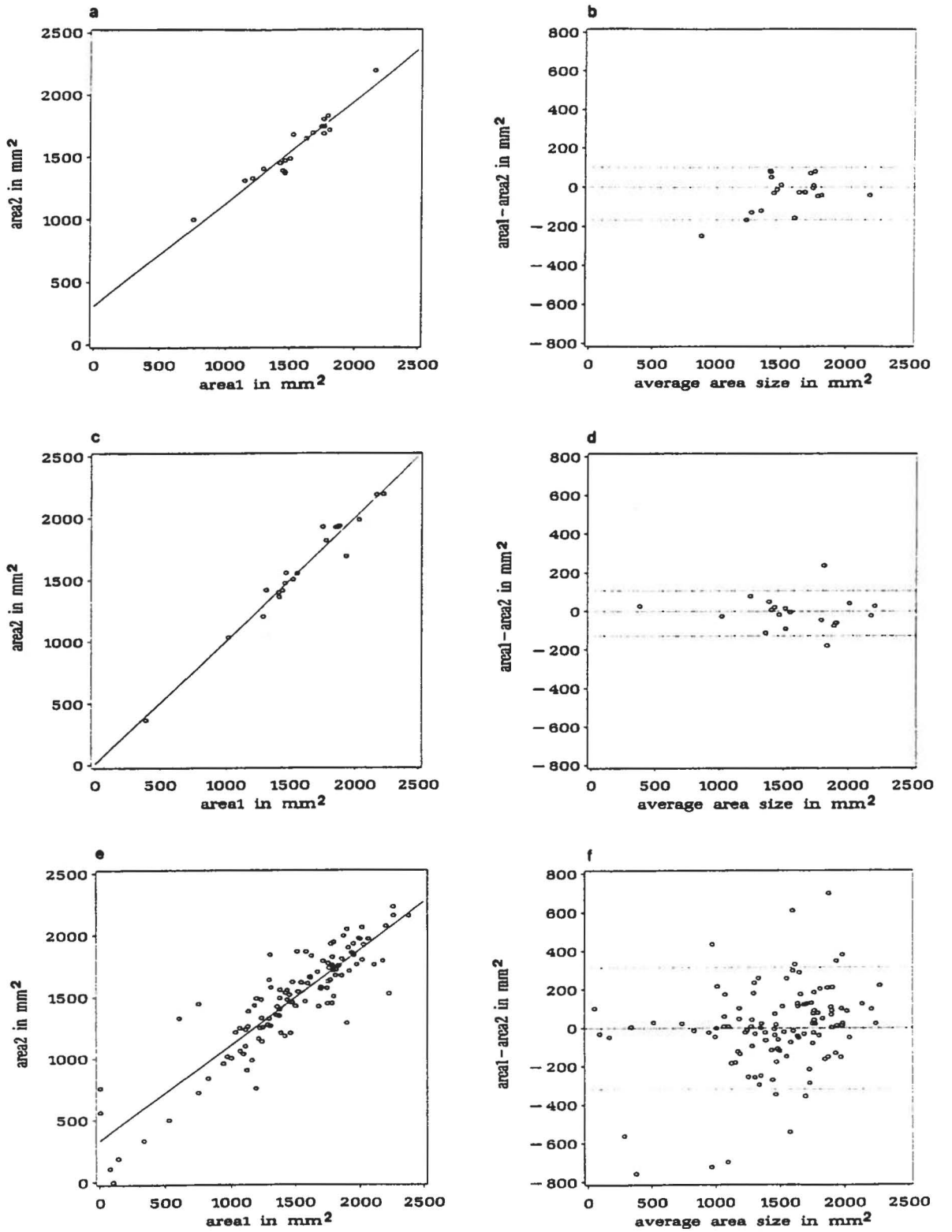

Fig. 8. Distributions of measured pneumatized areas in the temporal bones showing lines of equality, limits of agreement and differences against average. Upper and lower dotted lines are mean difference +/- 2 SD. a and b: Intra-observer variation for observer 1. c and d: Intra-observer variation for observer 2. e and f: Inter-observer variation for observer 1 and 2.

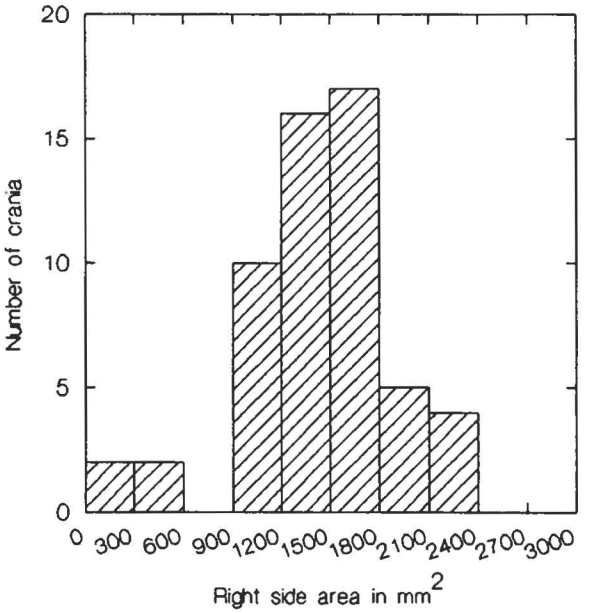

Fig. 9. Distribution of the right side pneumatized cell areas in the 56 historical Eskimo crania.

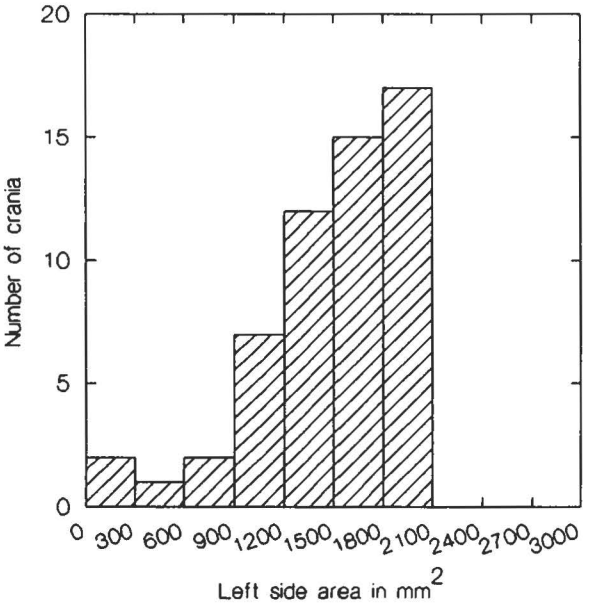

Fig. 10. Distribution of the left side pneumatized cell areas in the 56 historical Eskimo crania.

one significance, probably due to chance alone, was found (see Table 6).

Discussion

Previous studies of area and IMED using planimetrical measurements on X-rays of the temporal bones have not tested the accuracy and repeatability of the planimetrical methods used (Diamant 1940; Diamant et al. 1958; Arora et al. 1978; Sadé and Hadas 1979; Qvarnberg 1982; Tos and Stangerup 1984; Zaidi 1989). These factors were evaluated in blind trials in the present study, and no bias was found in either non-parametric or parametric tests. The graphical lines of equality between the observer's measurements were excellent and the distributions of differences against

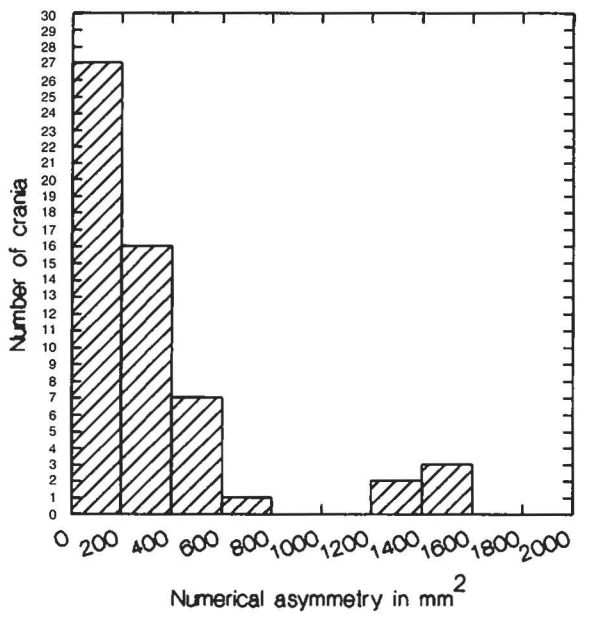

Fig. 11. Bilateral asymmetry in the 56 historical Eskimo crania.

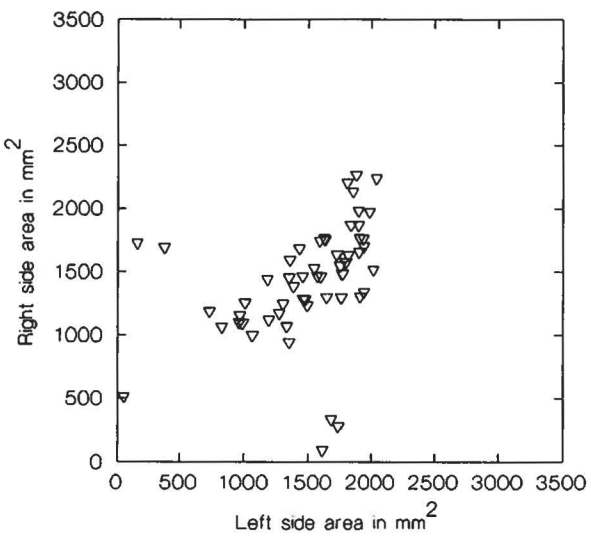

Fig. 12. Plot showing the area distribution of the 56 historical Eskimo crania.

Table 6. Significance of correlation between cranial measurements and size of left and right pneumatized areas using Spearman rank correlation test. R(s)= rank correlation coefficient. p = significance level.

Variables	Area right side		Area left side	
	R(s)	p	R(s)	p
M1 Maximal length	0.046	0.743	0.071	0.605
M8 Maximal breadth	–0.035	0.796	–0.148	0.276
M5 Basion-nasion	–0.260	0.156	0.182	0.179
M11 Biau. breadth	0.156	0.251	–0.012	0.929
M17 Basion-bregma	0.165	0.059	0.113	0.410
M40 Basion-prosthion	0.192	0.224	0.150	0.268
M48 Nasion-prosthion	0.287	*0.032	0.219	0.105
Cranial Index	–0.195	0.150	–0.247	0.067

averages of the two observers' measurements were small compared with the total area (see Fig. 8). This permitted subsequent studies to be done by a single observer. The analysis of the variance component model estimated the total mean variation to be 487.85 mm^2, the biological variation 438.52 mm^2, equalling 88% of the total variation, while the variation in the planimetric procedure (interobserver, intraobserver and technical error) was 158.29 mm^2, which accounted for only 12% of the total variation. This suggested that the method was reliable and confirmed that the pneumatized cell area varies considerably from individual to individual. A graphical examination of the variation in area also revealed that the variation was the same in small and large areas (see Fig. 8).

This study showed a rather high median or mean area compared with studies of adults of other races, even after correction for magnification (Diamant 1940; Arora et al. 1978; Zaidi 1989). Comparisons must however be treated with caution because of possible minor methodological dissimilarities (e.g. varying projection angles and X-ray distances). If the finding reflects a true difference, the cause of such a difference is unknown, but it may be due to genetic, racial or external factors. The degree of asymmetry was also higher in this study than in Diamant's normal material. This may partly be because Diamant's material probably did not include subjects with COM. In addition, the mucosa lining the cell system in living subjects is not present in skeletal material. However, this is considered to be of minor importance, since it is possible to distinguish bony structures from mucosa in X-rays.

Correlation between the area of pneumatization and the cranial dimensions has been reported (Turner and Porter 1922; Schulter-Ellis 1979; Zaidi 1989). In the present study there was no significant correlation between cranial dimensions and the pneumatized area, except for the right side area and the nasion-prosthion length (see Table 6). The latter result was ascribed to chance (mass significance) in view of the non-significant correlation on the other side and with all other facial measurements. When the Bonferroni correction was applied to the p-values of the correlations (7 * 0.032) this significance disappeared (Altman 1991). Similarly, there were no tendencies towards sexual dimorphism in the area, which indicates that the pneumatized area is determined by other factors.

As in Diamant's study (1940) the areas on the right and left side of each cranium showed high correlation (r(S) = 0.608), although five crania exhibited a high degree of asymmetry (see Figs. 11 and 12).

Tos and Stangerup (1985a) showed that asymmetry was highly correlated with IMED. In this study, five crania showed evidence of earlier IMED, when asymmetry is defined as bilateral area difference exceeding the mean plus two standard deviations (1087.56 mm^2) (Fig. 11). Varying rates of asymmetry (i.e. acellular mastoid process on one side and pneumatic mastoid process on the other side) in different human races have been reported by Turner and Porter (1922). As cellular appearance was not divided into different groups in this study, the findings could not be compared.

One cranium exhibited bilateral hypocellularity, which also correlates with known episodes of IMED (Diamant 1940; Diamant et al. 1958; Palva and Palva 1966; Arora et al. 1978; Sadé and Hadas 1979; Hussl and Welzl-Muller 1980; Lindeman and Shea 1980; Lindeman et al. 1981; Hug and Pfaltz 1981; Qvarnberg 1982; Tos and Stangerup 1984).

The study thus revealed that the pneumatized cell area in cranial material could be measured with acceptable accuracy and repeatability. The distribution of the pneumatized cell areas in cranial material showed characteristics similar to those of living subjects. Six (11%; 95% CI: 4.0% – 21.9%) of the 56 historical Eskimo crania examined showed evidence of previous exposure to IMED in childhood, when we extrapolate from the degree of asymmetry and bilateral hypocellularity. By comparison, the prevalence of COM in the present Eskimo population has been found to vary between 8% and 30% (Reed and Dunn 1970; Baxter and Ling 1974; Baxter 1977, 1983; Baxter et al. 1986; Pedersen and Zachau-Christiansen 1986, 1988).

CT scanning of historical Eskimo crania

Six of the historical Eskimo crania exhibited clear differences in the pneumatized cell areas. One of the six crania had pronounced bilateral hypopneumatization and five crania had pronounced asymmetry, so these six crania were assumed to have had IMED in childhood. If this were true, the crania would be expected to show morphological characteristics which could be revealed by CT scanning of the crania. In the following, the results of the gross examination, otomicroscopy and CT scans of each of the six crania are presented and commented.

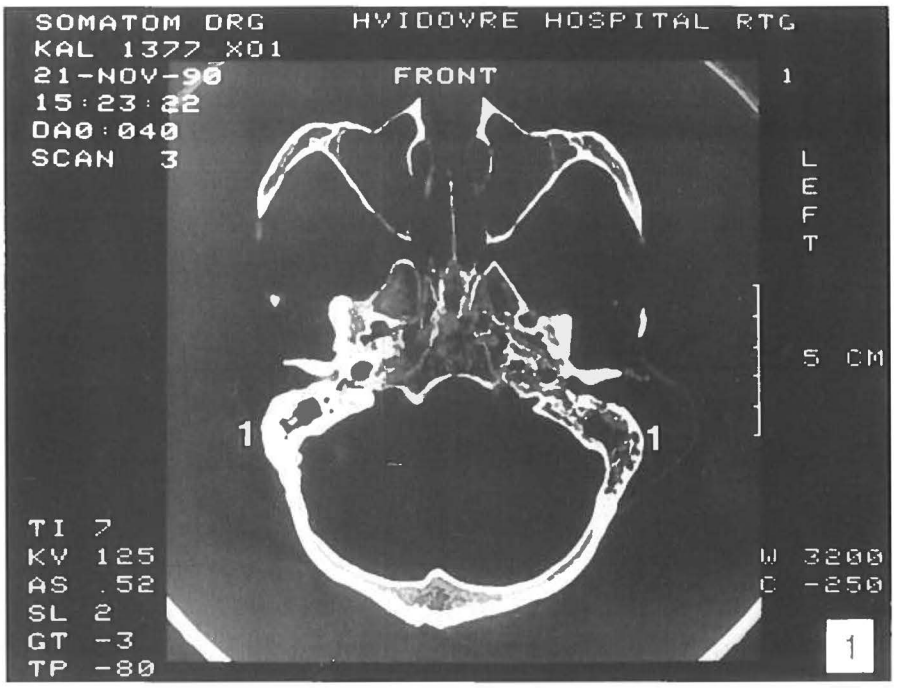

Fig. 13. CT-scan at the mastoid level of cranium no. 1. The cell systems on both sides are seen (1).

Cranium No. 1 (Figs. 13 – 15) KAL-1377X01
Gross examination and otomicroscopy showed no pathological signs. The planimetrical analysis showed asymmetry with an average-sized left area measuring 1684.50 mm^2, and a below-average area on the right side measuring 334.00 mm^2.

The CT scans showed a marked difference between the two sides in the mastoid air cells and the surrounding bone tissue. The left side had a well developed and clearly defined air cell system, with a fine trabecular structure (clearly seen in the magnification, Fig. 14). The right side showed much sclerosing, obliteration

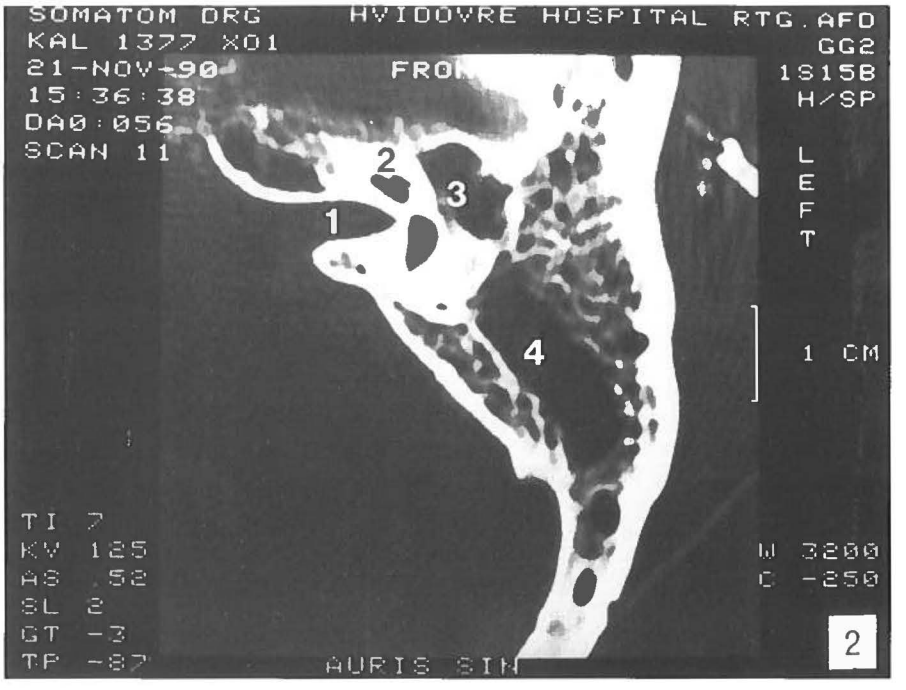

Fig. 14. The left temporal bone of cranium no. 1. seen in magnification. The scan was taken at the cochlear level. Different structures are marked. Meatus acusticus internus (1), cochlea (2), cavum tympani (3) and antrum mastoideum (4). The air cell system is well developed

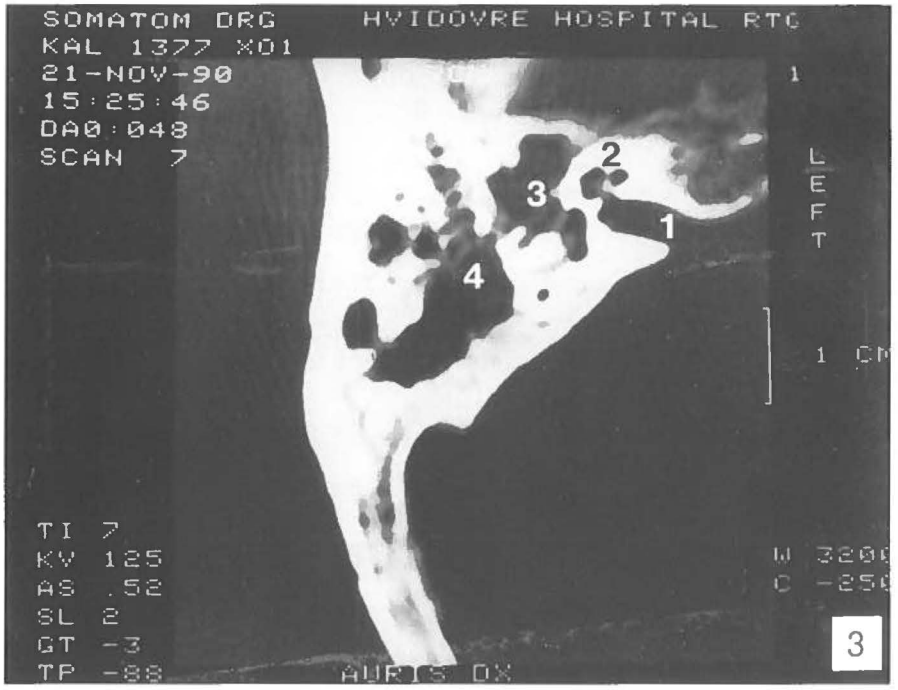

Fig. 15. The right temporal bone of cranium no. 1. seen in magnification. The scan was taken at the cochlear level. Meatus acusticus internus (1), cochlea (2), cavum tympani (3) and antrum mastoideum (4). The cell system displays sclerosing, obliteration and irregularity.

and irregularity of the air cell system, of which the remnants were seen as isolated circular spaces (Fig. 15). The mastoid antrum was well developed on both sides and the temporal bones were of almost the same thickness at the cochlear level, while the corticalis was thickened at the mastoid level on the right side.

Cranium No. 2 (Fig. 16) KAL-0263X01
Gross examination and otomicroscopy showed no pathological lesions. The planimetrical analysis showed asymmetry with an average-sized left area measuring 1738.00 mm^2, and a below-average area on the right side measuring 280.50 mm^2.

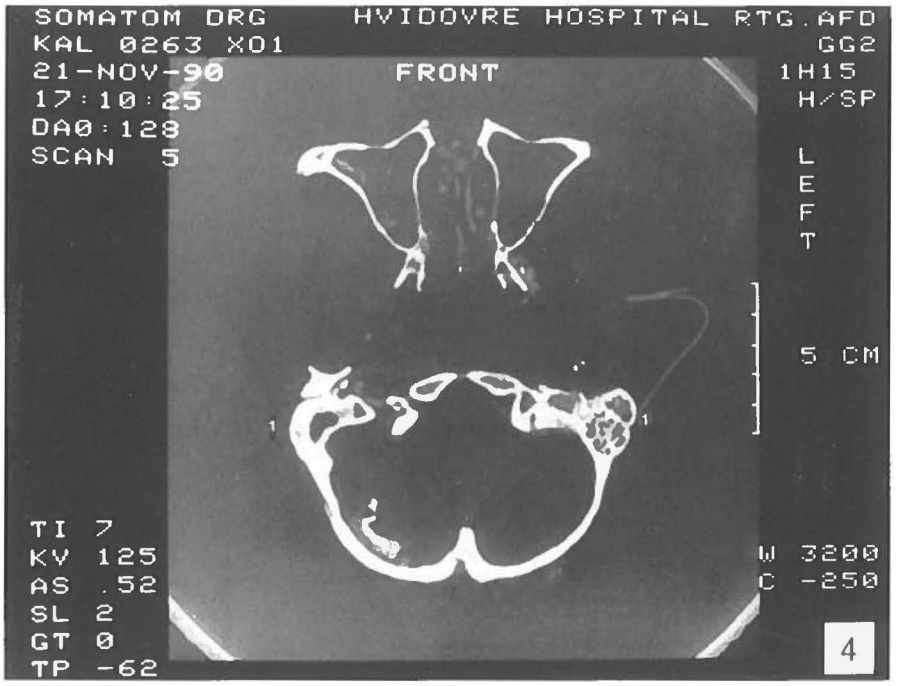

Fig. 16. CT-scan at the mastoid level (1) of cranium no. 2. The right side shows thickening of the corticalis.

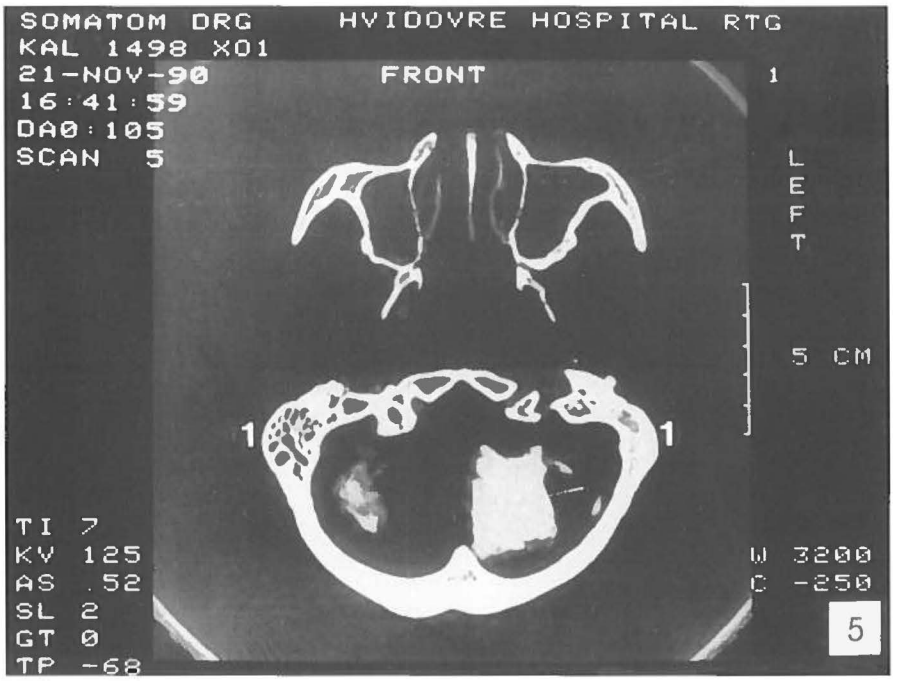

Fig. 17. CT-scan at the mastoid level (1) of cranium no. 3. The left side is sclerosed.

There was a marked difference in the bony structures of the middle ear and the air cell system. Compared with the left side, the right side showed sclerosing, obliteration and irregularity, with clearly reduced pneumatization. The corticalis surrounding the mastoid process was thickened. Only the mastoid antrum seemed to be intact.

Cranium No. 3 (Fig. 17) KAL-1498X01
Gross examination and otomicroscopy showed no pathological lesions. The planimetrical analysis showed asymmetry with a below-average left area measuring 164.00 mm^2, and an average-sized area on the right side measuring 1725.50 mm^2.

The two sides differed clearly: the right side was

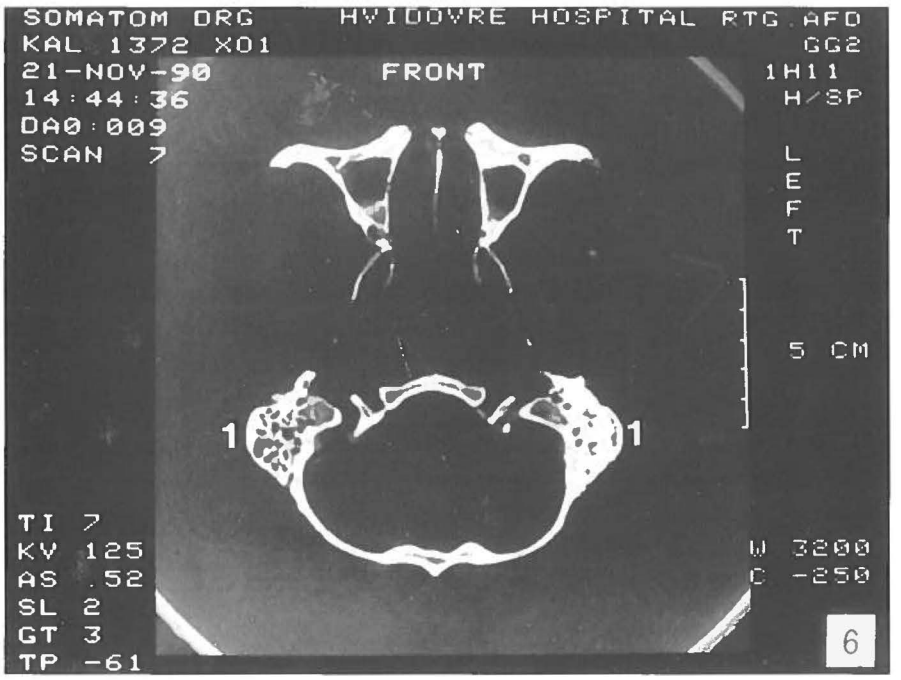

Fig. 18. CT-scan at the mastoid level (1) of cranium no. 4. The left side displays sclerosing and irregularity.

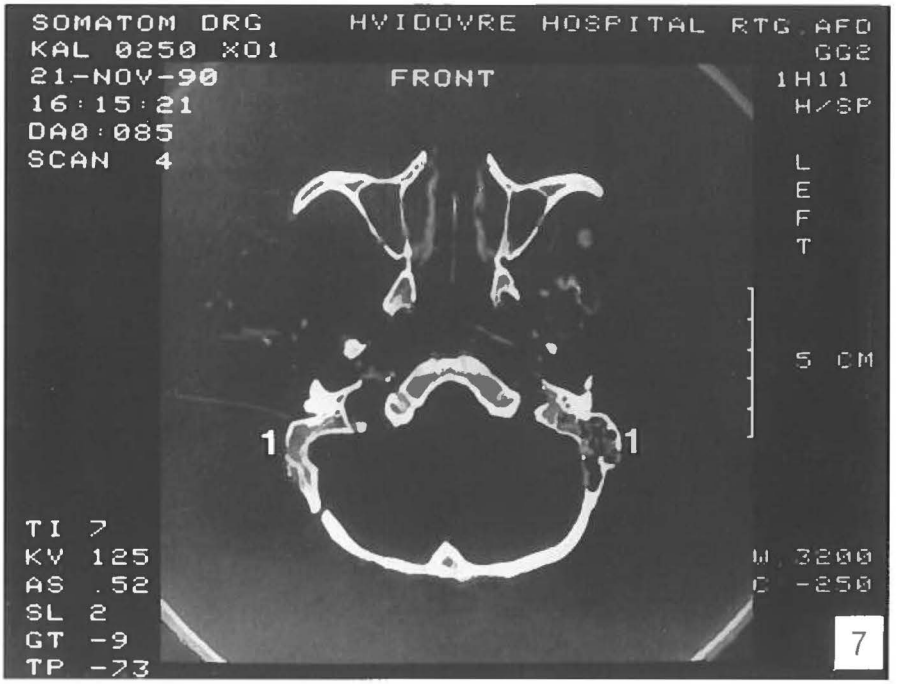

Fig. 19. CT-scan at the mastoid level (1) of cranium no. 5. The right temporal bone seems more narrow and the cell system resembles spongiosa compared to the left side.

seen as well pneumatized, whereas the left side was sclerosed, obliterated and had a thickened corticalis at the mastoid level. Practically no cells were seen on this side.

Cranium No. 4 (Fig. 18) KAL-1372X01
Gross examination and otomicroscopy showed no pathological lesions. The planimetrical analysis showed asymmetry with a below-average left area measuring 378.50 mm^2, and an average-sized area on the right side measuring 1690.50 mm^2.

The right side exhibited a well developed and clearly defined trabecular network and air cell system, compared with the left side, which exhibited

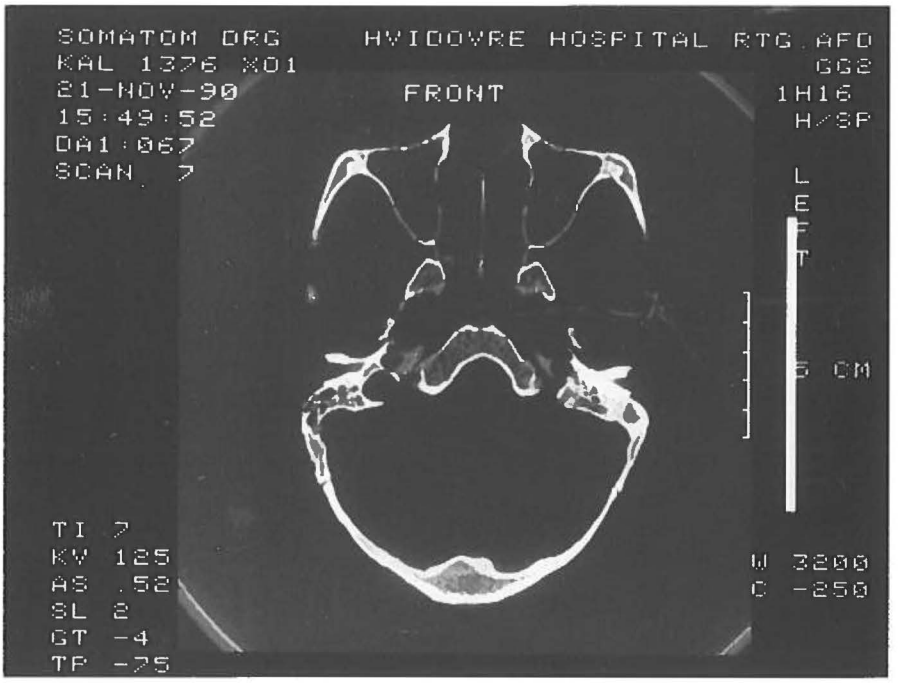

Fig. 20. CT-scan at the mastoid level (1) of cranium no. 6. The left side is sclerosed while the right side is well pneumatized.

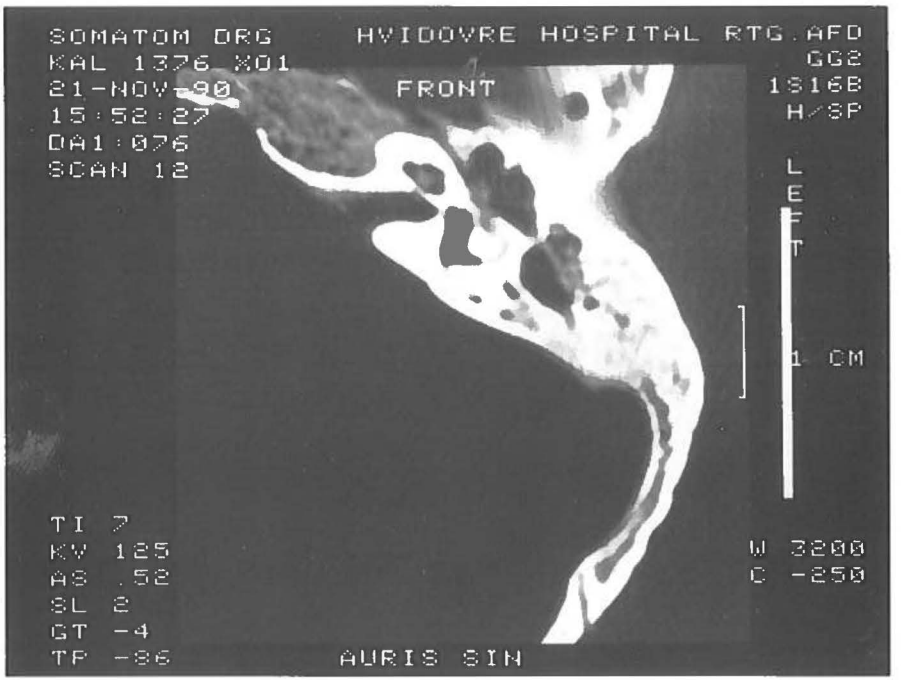

Fig. 21. The left temporal bone of cranium no. 6. seen in magnification. The scan was taken at the cochlear level. Sclerosing and obliteration of the cell system is clearly seen.

sclerosing, obliteration and irregularity. The corticalis did not seem thickened, and the antrum was normal.

Cranium No. 5 (Fig. 19) KAL-0250X01
Gross examination and otomicroscopy showed no pathological lesions. The planimetrical analysis showed asymmetry with a below-average right area measuring 92.50 mm^2, and an average-sized area on the left measuring 1613.00 mm^2.

The left side appeared normal, with a rather large air cell system. The bony structures of the right middle ear almost resembled spongiosa with very small

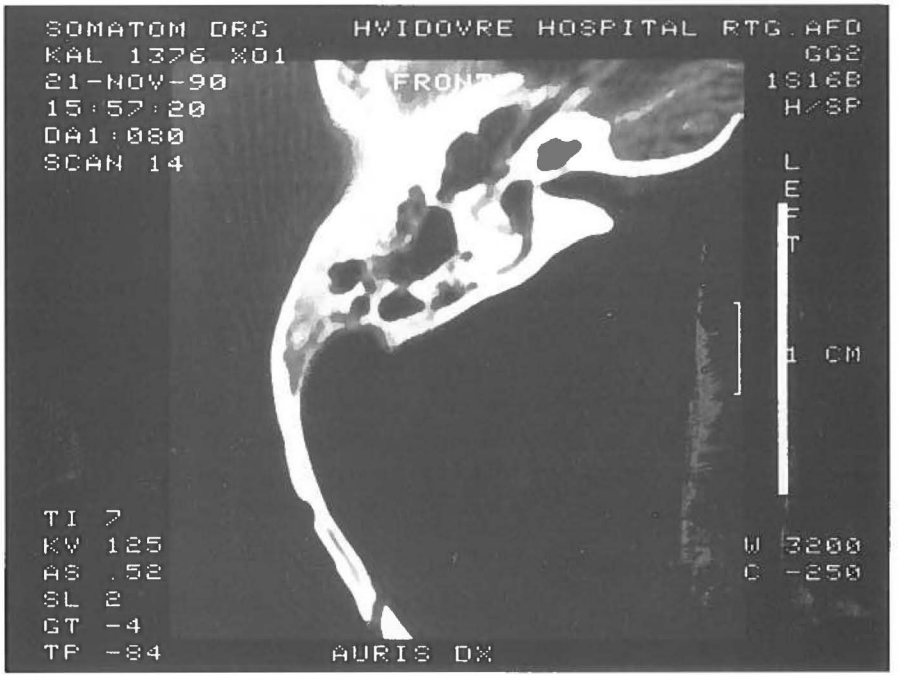

Fig. 22. The right temporal bone of cranium no. 6. seen in magnification. The scan was taken at the cochlear level and displays sclerosing, obliteration and irregularity of the cell system.

Table 7. Pathological changes as seen in CT-scans of the pneumatized cell system in the six crania suspected for IMED.

Crania KAL-no.	Pathology at: Gross anatomy; Otomicroscopy	Sclerosing of air cells	Obliteration of air cells	Irregulating of air cells	Corticalis thickening
1377X01	No	Yes	Yes	Yes	Yes
0263X01	No	Yes	Yes	Yes	Yes
1498X01	No	Yes	Yes	No	Yes
1372X01	No	Yes	Yes	Yes	No
0250X01	No	Yes	Yes	No	No
1376X01	No	Yes	Yes	Yes	Yes

cells, and the temporal bone did not appear as thick as on the left side. A widening in the lambdoid suture was seen on the right side, probably due to postmortal changes.

Cranium No. 6 (Figs. 20 – 22) KAL-1376X01
Gross examination and otomicroscopy showed no pathological lesions. The planimetrical analysis showed bilateral hypopneumatization of below-average area on both the left and right side, measuring 51.00 mm^2 and 513.50 mm^2 respectively.

In Fig. 20, taken at the upper mastoid process level, a difference in the degree of obliteration and sclerosing was seen. However, in the magnifications (Figs. 21 and 22), taken at the cochlear level, both sides exhibited a sclerosed and obliterated cell system, with a high degree of irregularity. The temporal bones and the corticalis were equally thickened on the two sides.

There was a well developed mastoid antrum in all the ears, and none of the crania showed signs of malignant tumours, cholesteatoma or craniofacial syndromes.

The results of the CT scans and the planimetrical analysis are summarized in Table 7.

Discussion

Gross examination showed normal maxillar, mandibular and facial structure, as well as normal dental development, and there were no pathological changes in the cranial vault: This make congenital disorders less likely as the cause of hypocellularity.

Normal otomicroscopy, apart from the absence of middle ear ossicles, was found in all six crania. Bruintjes (1990) examined middle ear ossicles for pathology but the ossicles were not examined in the present study because of post-mortal loss in several of the crania.

CT scanning of the temporal bones showed a high degree of bony sclerosing, cell obliteration, destruction of the cellular septae and irregularity of the cells. These pathological findings are identical to findings in patients with a history of severe IMED (Brøste 1931; Runström 1933; Friedmann 1957; Palva and Palva 1966). The alterations were all found on the sides in which the pneumatized cell area was small, i.e. on both sides in the bilaterally hypopneumatized cranium and on the hypopneumatized sides in the asymmetrical crania. This supports the correlation described by Tos and Stangerup (1985a) between the degree of asymmetry in the pneumatized cell system and IMED.

In the cranium with bilateral hypocellularity (Cranium No. 6), both sides showed sclerosing and cell obliteration at the cochlear level, but there was a fairly well pneumatized cell system in the right side at the upper mastoid level (Fig. 20). The difference in pneumatization at the mastoid level may indicate less virulent infections and/or fewer infections on the right side.

Cranium No. 5 exhibited a difference in the thickness of the temporal bones on the two sides, and had practically no air cells on the right side. This might suggest a congenital malformation without pneumatization of the right temporal bone. The mastoid antrum and the tympanic cavity were however normally developed, as was the cochlea. This does not exclude the possibility of a congenital malformation, but makes it less likely. Another explanation could be that IMED occurred neonatally, thereby arresting the development of the pneumatized cells and even to some degree arresting the growth of the temporal bone on this side.

These results accord with the environmental theory of the pneumatization of the temporal bone (see Introduction – The environmental theory). It is unlikely that the sclerosing and obliteration of the cells are hereditary. In particular, the irregularity of the cells indicates a secondary formation. However, the hypopneumatization may still be hereditary. This study does not give a definite answer to the question whether hypocellularity of the temporal bones is hereditary or environmental, but indicates that former infections can minimize the pneumatized cell area (i.e. by sclerosing and obliteration), as also found by Friedmann (1957) and Palva and Palva (1966).

The findings expected prior to the study were thus confirmed in all crania. This supports the view that the frequency of IMED in historical populations can be estimated from the pneumatized cell area of the temporal bones. However, this requires an examination of the pneumatized area distribution in a sample in which the prevalence of IMED in childhood is known. Furthermore, since this study concerned IMED in the Greenland Eskimos and since the relationship between IMED and small or asymmetrical cell areas has so far only been established in whites, this relationship had to be established in the Eskimos.

Table 8. Descriptive statistics of the right and left side pneumatized cell areas in the 34 modern Greenlanders. All values in mm^2.

Area size	Mean	SD	Median	Max.	Min.
Left	1292.85	588.22	1275.50	2738.00	123.00
Right	1332.82	651.99	1304.50	2647.00	88.00

Modern Greenlanders

According to the questionnaires answered by the 34 modern living Greenlanders and the medical records, nine respondents (26%) reported IMED in childhood (six females and three males), corresponding to 12 of 68 ears (18%). Objective signs of IMED were found in eight of the 12 tympanic membranes of respondents who reported IMED while no signs were found in non-IMED respondents.

The mean, standard deviation, median and range of the right and left pneumatized cell areas of the sample are shown in Table 8.

There was no significant difference in the frequency of IMED in females and males (Chi-square = 0.93, p = 0.34) and there was no sexual dimorphism in measured area among non-IMED subjects (z' = –0.662, p = 0.51).

The distribution of the pneumatized areas in the right and left temporal bones is shown in Fig. 23. A significant relationship was found, using non-parametric analysis, between the pneumatized area and history of IMED for each side (left side: z' = –2.711, p = 0.005; right side: z' = –2.530, p = 0.009).

The relationship between pneumatized area and history of IMED for each ear, including information from both sides and using the polychotomous logistic regression model, was highly significant (for $\gamma_1 = \gamma_2 = 0$, $p < 0{,}0001$, see page 17). This was due to an association between IMED and small areas (for γ_2, $p < 0.001$), as well as an association between unilateral IMED and pronounced individual asymmetry (for γ_1, p = 0.003). When the model was applied to the area for allocation purposes, eight subjects were designated as having had IMED in childhood (see Fig. 24).

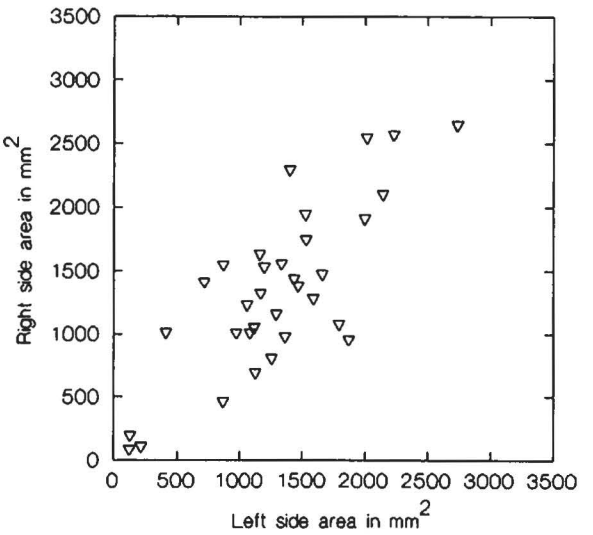

Fig. 23. Plot showing the distribution of pneumatized cell areas in the modern Greenlanders (N = 34).

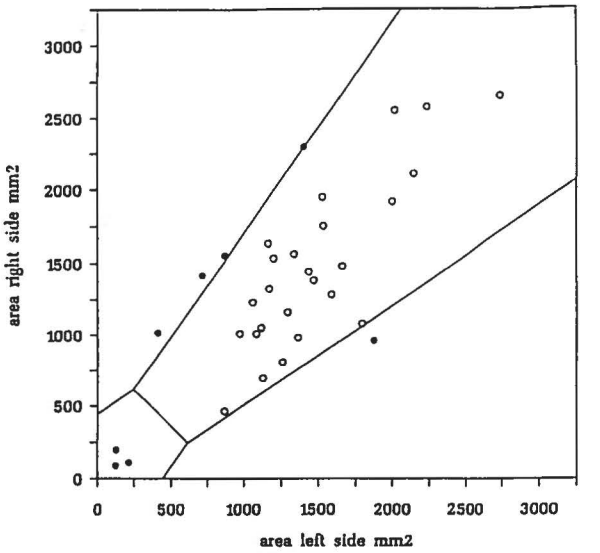

Fig. 24. Plot of the distribution of pneumatized cell areas in the modern living Greenlanders (N = 34) with the model allocation limits. Filled circles represent persons denoted by the model as having had IMED (N = 8). Open circles represent persons without IMED as denoted by the model (N = 26).

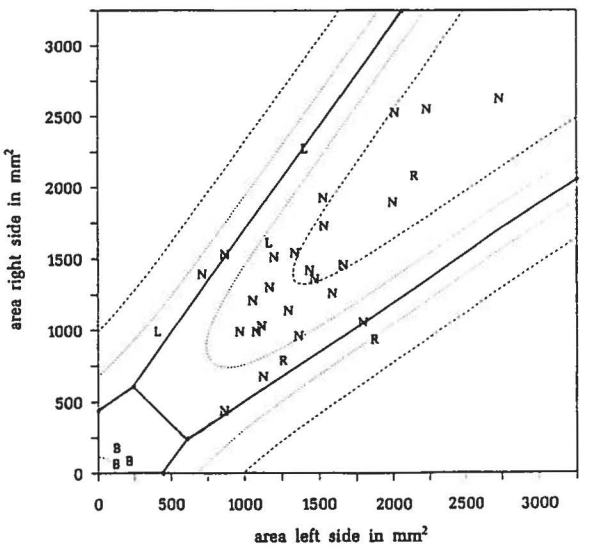

Fig. 25. Plot of the pneumatized area distribution of the 34 modern living Greenlanders, their reportation of former IMED in childhood and the model risk estimate levels for IMED. The solid lines show the allocation limits of the model. The dotted lines show 95% (– – –) and 75% (.....) allocation confidences of the model. IMED in both ears (B), IMED in left ear (L), IMED in right ear (R) and normal in both ears (N).

Table 9. True categories versus model allocation from pneumatized area size.

True category	Allocation to category by model 1	2	3	4	Total
1 = normal both ears	23	2	0	0	25
2 = IMED left ear	1	2	0	0	3
3 = IMED right ear	2	0	1	0	3
4 = IMED both ears	0	0	0	3	3
Total	26	4	1	3	34

Sensitivity: 6/9 = 67% (95% CI: 30% – 93%)
Specificity: 23/25 = 92% (95% CI: 74% – 99%)
Positive predictive value: 6/8 = 75% (95% CI: 35% – 97%)

The ability of the polychotomous logistic regression model to characterize the modern Greenlanders correctly is shown in Table 9 and graphically in Fig. 25.

Using the model for classification of the historical Eskimo sample, we classified six crania (11%) as having had IMED (see Fig. 26). The occurrence of IMED could also be considered as a Bernouilli-distributed variable with an estimated probability which was the sum of the three group probabilities (++,+–,–+) (see the section "Statistical methods"). This gave an estimated number of nine to ten occurrences of IMED with CI between five and 14, thus including the above finding of six diseased crania.

Discussion

The age span of subjects, from 14 to 65, was considered acceptable, as it is generally agreed that the development of the pneumatized cell system in the temporal bone has terminated before the age of 14 (Rubensohn 1965; Palva and Palva 1966). Recalling IMED in childhood may be difficult, but this is probably of minor importance in the study, since only the severer diseases such as COM, CTD or RAOM are associated with small pneumatized cell areas (Diamant 1940; Friedmann 1957; Diamant et al. 1958; Palva and Palva 1966; Arora et al. 1978; Sadé and Hadas 1979; Hussl and Welzl-Muller 1980; Hug and Pfaltz 1981; Tos and Stangerup 1984).

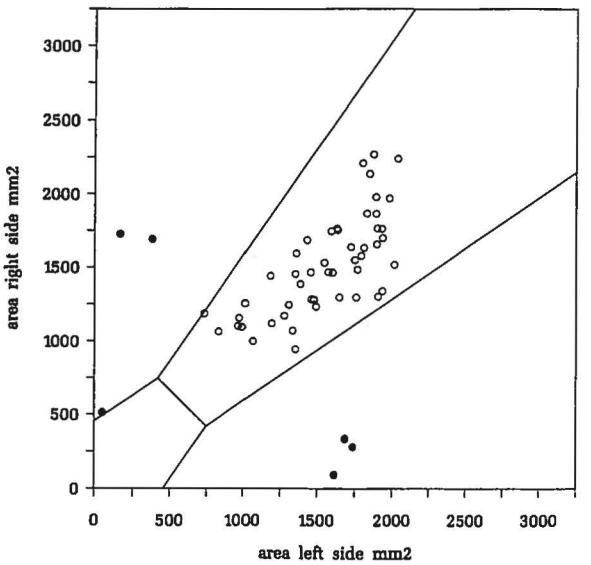

Fig. 26. Plot showing the distribution of the pneumatized cell areas in the historical Greenland Eskimo sample with the model allocation limits (N = 56). Filled circles represent crania denoted by the model as having had IMED (N = 6). Open circles represent crania without IMED as denoted by the model (N = 50).

The material consisted of hospitalized modern Greenlanders and may to some extent be considered selective. According to the questionnaires and medical histories, nine subjects (26%) had experienced episodes of IMED in childhood. Three of these had COM. Previous studies have shown prevalences of COM between 8%-30%, and among children less than 3 years old 75%-90% have had AOM in Eskimo areas (Reed and Dunn 1970; Baxter and Ling 1974; Baxter 1977, 1983; Baxter et al. 1986; Pedersen and Zachau-Christiansen 1986, 1988). Thus the percentage of 26% who had suffered from IMED (i.e. COM and/or recurrent AOM) in this study was probably representative of the total population and the selection bias is therefore reduced. A larger sample size would have been preferred, but because of the present ethical restrictions additional X-rays of subjects without ear disease could not be obtained.

Sequelae were found in eight of 12 tympanic membranes in ears with IMED, reflecting the fact that the tympanic membrane is able to heal without scarring, as also found by Tos (1982) and Tos et al. (1984). Sequelae in the tympanic membrane were found in all ears with very small pneumatized cell areas (< 400 mm^2).

It can be seen from Fig. 25 that all the ears with very small areas (i.e. < 400 mm^2) have had IMED. It can also be seen that IMED was reported in subjects with areas as large as 2105 mm^2. According to the environmental theory of pneumatization (see Introduction), this variability can be explained by differences in disease virulence, chronicity of the disease, age at episode of IMED, and treatment efficacy. According to the hereditary theory of pneumatization, the very small cell areas caused by the natural variation in a biological population tend to be important for disease virulence and chronicity. The present study of modern Greenlanders confirmed the close relationship between IMED and hypocellularity, irrespective of possible causal relationship.

The non-parametric analyses of the relationship between pneumatized area and IMED showed significance on each side. In order to express the significance of the relationship between IMED and small area with only one test statistic and to include less severe cases of IMED, the polychotomous logistic regression model was used to calculate the risk of earlier IMED, given a specific pair of areas. The ability of the model to allocate the individuals to the correct

Table 10. Descriptive statistics of the right side pneumatized cell areas in the prehistorical Eskimo sample. All values in mm^2.

	Male			Female		
Region	NE	SE	W	NE	SE	W
N	13	20	21	16	22	35
Mean	1957.39	2099.45	1676.10	1687.88	1775.41	1550.91
SD	391.94	452.79	399.18	333.26	506.12	477.76
Median	1979.00	2220.00	1691.00	1694.50	1884.00	1454.00
Maximum	2487.00	2799.00	2442.00	2294.00	2502.00	3050.00
Minimum	1330.00	1120.00	960.00	920.00	135.00	861.00

Table 11. Descriptive statistics of the left side pneumatized cell areas in the prehistorical Eskimo sample. All values in mm^2.

	Male			Female		
Region	NE	SE	W	NE	SE	W
N	13	20	21	16	22	35
Mean	1995.15	2143.70	1726.43	1643.25	1791.77	1497.91
SD	462.36	412.69	527.90	410.07	351.93	475.74
Median	2092.00	2196.00	1791.00	1679.50	1891.00	1523.00
Maximum	2689.00	2849.00	3093.00	2417.00	2326.00	2662.00
Minimum	1321.00	1229.00	852.00	907.00	1218.00	0.00

group was acceptable, as shown in Table 9 and graphically in Fig. 25. The model was able to find between two and three subjects with IMED who would not have been found by simple arbitrary segregation (the subjects with areas close to the allocation limits). Fig. 25 also shows the confidence with which allocation to any of the four groups was made.

The sensitivity, specificity and positive predictive value (see Table 9) suggest that a reliable minimum value can be obtained for the incidence of IMED in an anthropological sample. Since the aim is to estimate the incidence in a population and not in a single individual, this estimated value will also approximate the true value, because false negatives tend to be balanced by false positives. Because of the limited sample size, the confidence intervals – especially for sensitivity and positive predictive value – are wide.

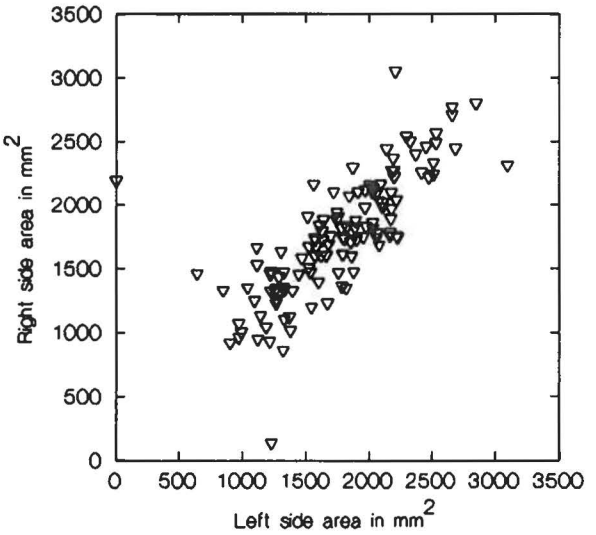

Fig. 27. Plot showing the distribution of the pneumatized cell areas in the prehistorical Eskimo sample (N = 127).

When the model was used on the historical Eskimo material, six crania (11%) were designated as having had IMED. These six crania were identical to those identified as having had IMED in the pilot study and the CT scanning study in which identification was based on an arbitrary correlation between IMED and bilateral asymmetry of the pneumatized areas, and on morphological evidence as seen on CT scans.

We conclude that small or highly asymmetrical pneumatized cell areas are closely related to occurrence of IMED in childhood in Greenlanders as well as others, and that the statistical model is able to estimate the frequency of IMED from cases with unilateral as well as bilateral small pneumatized areas of the temporal bones in historical crania. This can be done more precisely than with previous techniques, especially when the distribution of areas is wide.

In order to study the frequency of IMED in prehistoric Greenland, the classification procedure was applied to a large sample of Eskimo crania originating from different geographical regions of Greenland and dating from before the modern colonization of Greenland in 1721 AD.

Prehistoric Eskimos

There was no significant difference in sex ratio between the W, SE and NE regions (Chi-square = 1.09, p = 0.607) (see Table 2).

The pneumatized areas of the 127 individuals were distributed as shown in Fig. 27. The right and left pneumatized areas showed a high correlation; r(S) = 0.833.

The mean, standard deviation, median and range of the right and left pneumatized cell areas of the sample are shown in Tables 10 and 11.

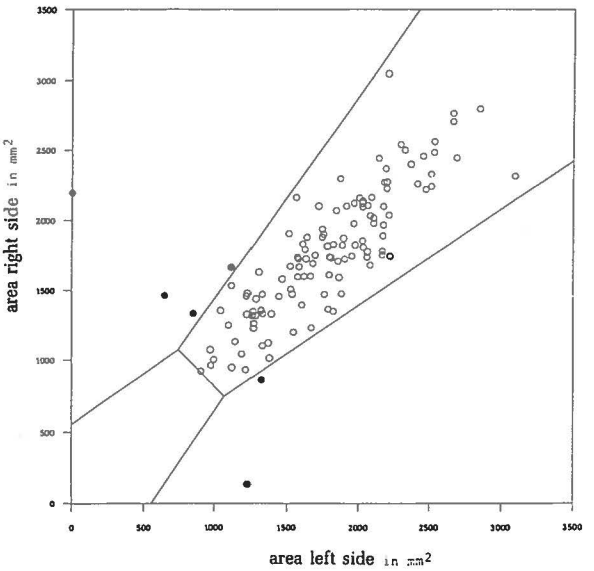

Fig. 28. Plot showing the distribution of the pneumatized cell areas in the prehistorical Greenland Eskimo sample with the model allocation limits after transformation of data into Z-scores (N = 127). Filled circles represent crania denoted by the model as having had IMED (N = 6). Open circles represent crania without IMED as denoted by the model (N = 121).

Table 12. Pneumatized cell areas in crania designated by the model as having had IMED.

Region	Sex	Area size in mm² Right	Left
SE	F	135.00	1231.00
NE	F	1664.00	1116.00
W	F	861.00	1322.00
W	F	1460.00	648.00
W	M	1331.00	852.00
W	F	2192.00	0.00

Table 13. Median area sizes in mm² according to region, n = 121 (all non-IMED) and the regional differences in area size by sex (Kruskall-Wallis test).

	NE	SE	W	p
Males	N = 13	N = 20	N = 20	
Left area	2092.00	2196.00	1817.00	< 0.02
Right area	1979.00	2220.00	1720.00	< 0.02
Females	N = 15	N = 21	N = 32	
Left area	1782.00	1902.00	1559.00	= 0.05
Right area	1725.00	1889.00	1424.00	< 0.01

The polychotomous logistic regression model designated six of 127 crania (= 4.7%; 95% CI: 1.8% – 10.0%) as having had IMED, all unilateral (see Fig. 28 and Table 12). The six crania were distributed as follows: four of 56 crania from the W (7%; 95% CI: 2.0% – 17.3%); one of 42 crania from the SE (2.4%; 95% CI: 0.1% – 12.6%); and one of 29 crania from the NE (3.5%; 95% CI: 0.1% -17.8%). Five were females and one was a male.

On the whole, the pneumatized cell areas were bilaterally significantly larger in non-IMED males than in non-IMED females (median right side: 1872.00 mm² for males, 1690.00 mm² for females, z'= 2.965, p = 0.003 (two-sided); median left side: 2030.00 mm² for males, 1645.00 mm² for females, z'= 3.547, p < 0.001 (two-sided)). An ANOVA test for difference between the areas in non-IMED males and females confirmed this (right side: p < 0.005 and left side: p < 0.001). The R^2 explanation ratios of sex to area

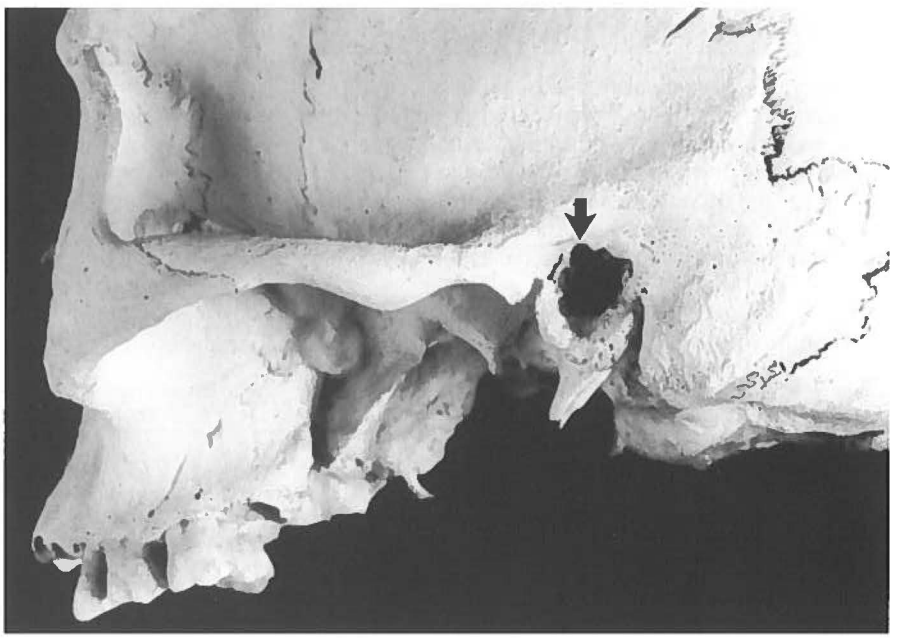

Fig. 29. Photomicrograph of a female prehistorical Greenland Eskimo crania from the W. The medial upper part of the external ear canal is eroded and ante-mortal bone-remodelling is visible (arrow).

Table 14. Median values of the cranial variables and the regional differences in cranial variables by sex (Kruskall-Wallis test). * N = 12, ** N = 34.

	Male				Female			
Region	NE	SE	W	p-value	NE	SE	W	p-value
N	13	20	21		16	22	35	
Maximal length (mm)	187.50	186.50	188.00	0.640	179.33	179.50	181.00	0.511
Maximal breadth (mm)	136.50	132.91	133.00	0.036	133.15	130.50	**131.50	0.235
Basion-nasion (mm)	*104.25	105.75	107.00	0.101	96.59	100.50	**99.00	0.041
Basion-bregma (mm)	137.50	138.75	139.00	0.231	129.50	135.00	134.00	0.012
Cranial index (%)	72.80	71.32	70.19		73.80	73.23	73.25	

Table 15. Correlation between cranial variables and pneumatized area sizes of the right and left temporal bones using Spearman rank correlation test, corrected for ties and two-sided. N = 121, representing complete and non-IMED crania. * N = 120, ** N = 119.

	Area right side		Area left side	
Measurements	R(s)	p	R(s)	p
Maximal length	0.065	0.48	0.078	0.28
Maximal breadth*	0.045	0.62	0.104	0.22
Basion-nasion**	0.202	0.03	0.224	0.02
Basion-bregma	0.212	0.02	0.198	0.03

were however low (right side: 6.7% and left side: 10.5%).

Regionally, the areas differed significantly in both non-IMED males and non-IMED females, as seen in Table 13. The male and female crania from the W have the smallest areas.

This trend was confirmed when an ANOVA test was done on the data for non-IMED subjects. The regions explained between 7.6% and 16.1% (R^2) of the variation in area among the three regions.

The otological examination of the non-IMED crania revealed no pathological changes, while antemortem bone destruction with surrounding bone remodelling in the innermost part of the external ear canal was found in one of the six IMED crania (see Fig. 29).

The crania were measured to examine whether differences in cranial morphology could explain the differences in the area. In Table 14 the median values are shown by sex and geographical region. In two crania, it was not possible to measure the basion-nasion distance, and in one cranium the maximum breadth could not be measured because the cranium was incomplete.

There was a significant regional difference in the maximum breadth for males (Table 14): the males from the NE were wider than males from the two other regions. There were significant regional differences in the basion-nasion and basion-bregma measurements for females: the NE females had the smallest median sizes in both cases (Table 15).

The coefficients of correlation between the measured areas and the cranial variables are shown in Table 15. There was a significant but small correlation between both the right and the left side areas and the basion-nasion and the basion-bregma measurements.

However, in a multiple regression analysis using all cranial measurements to describe area, no significant effects were found, and the cranial measurements could only explain 5 – 7% of the variation in area (see Table 16).

Discussion

The pneumatized cell areas were larger in the prehistoric Eskimo material than in the historical Eskimo material and the modern Greenlanders, and when compared with data in studies of other ethnic populations (Diamant 1940; Arora et al. 1978; Zaidi 1989). This required a conversion of the data into Z-scores (see the section "Statistical methods"). The high correlation between right and left areas seen in Figure 27 resembled the findings in the above-mentioned studies.

The frequency of IMED was 4.7%. This is lower than the present epidemiological figures for IMED among the Eskimos in the Arctic, where figures for COM vary between 8-30% (Reed and Dunn 1970; Baxter and Ling 1974; Baxter 1977, 1983; Baxter et al. 1986; Pedersen and Zachau-Christiansen 1986, 1988). The model classified six crania as having had IMED, all unilaterally (see Fig. 28 and Table 12). Four were from the W where there may have been sporadic contacts with people like whalers and Norse-

Table 16. Multiple regression analysis of all cranial measurements on the left and right pneumatized areas. N = 118, three excluded due to incompleteness. Adjusted R^2 = 2.1%. R^2 = 5.4% for right side, R^2 = 6.7% for left side.

	Coefficient		Standard error		T-test		p(two tailed)	
Area Variable	Left	Right	Left	Right	Left	Right	Left	Right
Constant	–583.45	230.06	1502.93	1521.60				
Basion-bregma	15.883	16.901	9.975	10.099	1.592	1.674	0.11	0.09
Basion-nasion	10.781	8.864	10.624	10.756	1.015	0.824	0.31	0.41
Maximal breadth	9.467	3.530	9.422	9.539	1.005	0.370	0.31	0.71
Maximal length	–11.600	–11.530	8.287	8.390	–1.400	–1.374	0.16	0.17

men in the past. One was from the SE region and one from the NE region. Both these regions are believed to have been totally isolated from the outside world. The cranium with IMED from the NE region had a relatively large pneumatized area (1116 mm^2) and lay close to the classification limit (Table 12 and Fig. 28). However, given the asymmetry and the conversion, this cranium had been designated as having had IMED. A test of the strength of the classification limits was therefore done (see the section "Statistical methods").

The otological examination of the prehistoric Eskimo material showed ante-mortem unilateral destruction with surrounding bone remodelling of the external ear canal in relation to the tympanic cavity in a female cranium from the W (see Fig. 29). The pathology resembles that caused by cholesteatoma, but cancer of the external ear canal is another possibility. However, cholesteatoma seems more likely, because the pneumatized area was zero, which strongly indicates IMED in childhood. There were no other pathological signs in the cranium.

The results showed sexual dimorphism in the pneumatized area, as males had larger areas. Significant regional differences in both right and left area were found for males as well as females: the crania from the W had the smallest median areas and the crania from the SE had the largest median areas (see Tables 10, 11 and 13). The ANOVA tests confirmed this, but the explanation ratios were low. It thus seemed interesting to investigate whether the variation was due to differences in cranial morphology.

The crania from the NE were wider (maximum breadth) but not as high (basion-nasion and basion-bregma) as crania from the W and SE regions, where the crania were similar (see Table 14). In a larger sample of Eskimo crania including the present sample the same results were found (Jørgensen 1953). The difference in cranial morphology accords with the theory of Eskimo migration in Greenland, which states that from the same point of entry in the Thule area, the W and SE Eskimos migrated down along the west coast and up the south east coast while the north east Eskimos migrated north of Greenland and down the north east coast (Jørgensen 1953; Laughlin and Jørgensen 1956; Koch 1989).

The correlations between the pneumatized areas and the height of the neurocranium (basion-nasion and basion-bregma distances) were significant but small, as shown in Table 15, and were neutralized by the Bonferroni correction (Altman 1991). To see whether the areas could be predicted to any extent from the cranial measurements a multiple regression analysis was done (Wilkinson 1990). All cranial variables were included in the test in order to look for strong effects. The analysis showed no significant effects, because the cranial variables are intercorrelated, so the effect on area is shared. The cranial variables taken together only explained 5 – 7% of the variability in the areas (see Table 16). There was thus no significant influence of cranial morphology on the pneumatized area. Whether the differences in area were due to ethnic differences or to more frequent URI and SOM in childhood could not be evaluated from the present data, but the lowest median area was found in the region with the highest frequency of IMED.

Table 17. Frequency of IMED in the three samples, as denoted by the polychotomous logistic regression model with CI, in %.

Sample	N	IMED frequency		95% binomial CI
Prehistoric	127	6	4.7%	1.8 – 10.0
Historic	56	10	17.9%	8.9 – 30.4
Modern	34	8	23.5%	10.8 – 41.2

The study showed that IMED, and probably cholesteatoma, occurred in prehistoric Greenland, including the isolated areas. The sample was too small to estimate any regional differences in the frequency of IMED, although IMED seemed to have occurred more frequently among people in the west, where there was a risk of infection from sporadic contact with Norse or later Europeans. The relatively low frequency of IMED (4.7%) in this prehistoric Eskimo sample compared with present-day epidemiological figures for IMED in Greenland, and the relatively large median area in prehistoric times, may both imply that there was less infection in Greenland before colonization. Finally, cranial morphology as a genetic indicator could not explain the variation in pneumatized cell areas.

Comparison of the three samples

The pneumatized cell area distributions among the modern Greenlanders, historical Eskimos and prehistoric Eskimos are shown in Figure 30 (a,b,c), which also shows the model classification limits for IMED

Table 18. Descriptive statistics of right and left side pneumatized cell areas in the three samples of non-IMED crania or persons. All values in mm^2. One-way ANOVA test for difference between the three area distributions; Right side: $F = 8.420$, $df = 2$, $p < 0.001$; Left side: $F = 9.785$, $df = 2$, $p < 0.001$.

Sample	Right side areas				Left side areas			
	Mean	SD	Max	Min	Mean	SD	Max	Min
Prehistoric	1779.6	450.4	3050.0	920.0	1801.9	449.7	3093.0	907.0
Historic	1554.0	330.8	2270.0	999.5	1560.2	330.2	2038,5	732.0
Modern	1449.5	569.6	2647.0	464.0	1470.5	449.8	2738.0	863.0

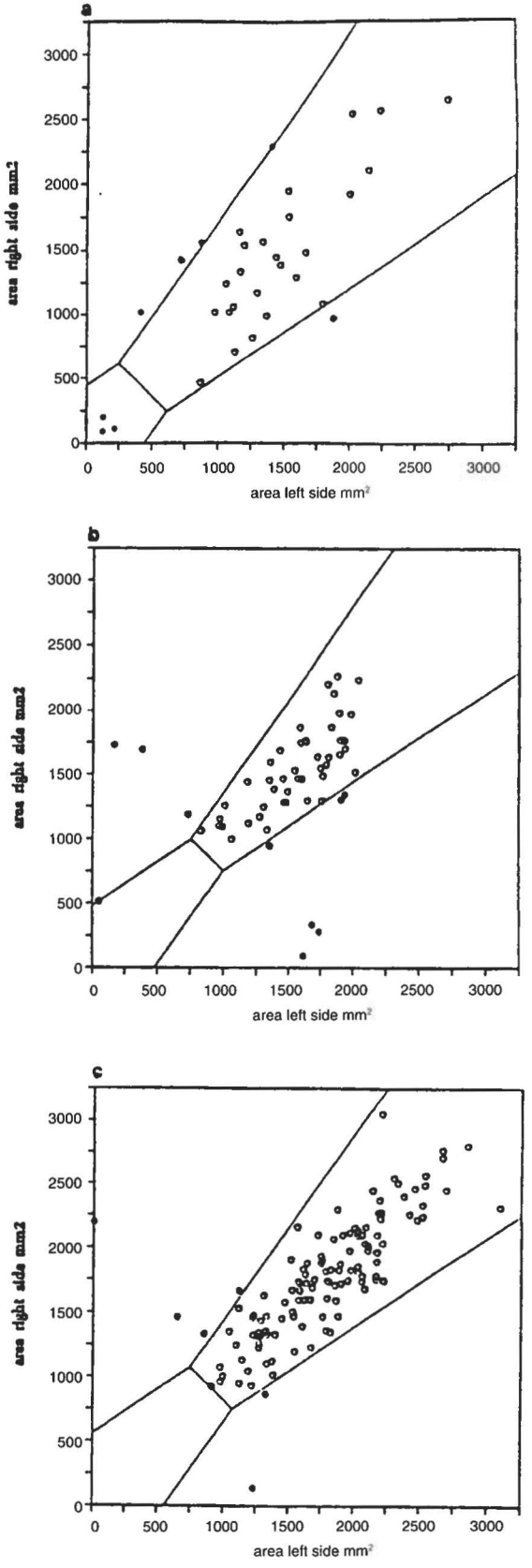

Fig. 30. The distributions of the three samples and model allocation limits after transformation of data to Z-scores. a: The modern Greenlanders (N = 34). b: The historical Greenland Eskimo sample (N = 56). c: The prehistorical Greenland Eskimo sample (N = 127). Filled circles represent persons / crania denoted by the model as having had IMED. Open circles represent persons / crania without IMED as denoted by the model.

after Z-score conversion. The IMED frequencies in the samples as calculated by the model are shown in Table 17. There was a statistically significant difference in IMED frequency among the samples (X^2 = 13.19, $p < 0.002$ (two-tailed)).

The descriptive statistics for area distribution among non-IMED subjects are listed in Table 18 together with the differences in area among the samples.

Discussion

The results of this study indicate an increasing secular frequency of IMED in the Greenland Eskimos and thus also an increasing frequency of URI. However, this interpretation does not allow for differences in infant and childhood mortality rates. Since infant and childhood mortality rates are known to be lower for the modern Greenlanders than for the historical Eskimos (Oldendov 1942; Bjerregaard and Misfeldt 1992), while we have no knowledge of mortality rates for prehistoric Eskimos, the results may rather reflect a more substantial increase in IMED frequency after the colonization of Greenland in 1721 than actually observed, and possibly a minor decrease in modern Greenland. This accords with medical reports on morbidity in general from the seventeenth and eighteenth centuries, and with some thought-provoking archaeological reports on the general social decline of the Eskimo societies in the same period (Meldorf 1907; Bertelsen 1940; Gad 1976; McGhee 1994).

The observed significant diachronic decrease in cell area (the mean and median values were bilaterally higher in the prehistoric and historical Eskimo materials than in the modern Greenlanders, even when corrected for IMED) may either be ascribed to an increased frequency of IMED and URI or to increased genetic admixture with Europeans in the present Greenlandic population. However, in the study of the prehistoric Eskimos from different parts of Greenland, variation in cranial morphology, also a genetic marker, could not explain the great variability in pneumatized cell areas. Furthermore, in this study the median area was found to be lowest in the region with the highest frequency of IMED. Compared with the modern Greenlanders, the prehistoric and historical Eskimo samples exhibited more distinct area distributions – with either very small or large pneumatized areas (see Figs. 30 a,b,c). This may reflect the effect of modern antimicrobial treatment of IMED, as suggest-

ed in a previous study (Gregg and Steele 1982). These observations thus accord with the supposition that IMED causes a decrease in cell area.

General discussion

The general health of past populations as assessed from anthropological skeletal material has traditionally been described by markers such as cribra orbitalia (porotic hyperostosis), which presumably reflects iron-deficiency anemia; dental enamel hypoplasia, which presumably reflects bouts of illness or dietary deficiency inhibiting enamel formation in growing teeth; and the so-called Harris's lines (transverse lines in long bone radiographs), which presumably indicate periods of growth arrest (Brothwell and Sandison 1967). However, many problems are encountered with these indicators (Larsen and Milner 1994; Lynnerup 1995). In the present study these indicators were not evaluated systematically, as this was not the purpose of the study. However, no cases of cribra orbitalia were found in the Greenland Eskimo skeletal material, and the postcranial material was known beforehand to be too small a sample for examination of Harris's lines. As food shortages are presumed to have occurred periodically in ancient and recent Greenland, any attempt to distinguish enamel hypoplasia caused by dietary shortage or disease in the Greenland Eskimo skeletal material would be close to pure guesswork. The examination of IMED, which is closely related to URI, may thus help to describe the general health of the population in the past. In addition, the method can be used in blind trials. Observation of gradual fluctuations in frequencies of pathological changes would be very relevant in the study of secular trends in skeletal biology. Analyses using a general disease marker such as IMED could contribute to the understanding of ancient societies by providing more information on the population as a whole and its general state of health than the simple listing of various (usually rare) diseases. IMED is known to occur worldwide with almost similar clinical manifestations, so the use of the method on anthropological material from other parts of the world would be an important tool in evaluating the transference capability and benefit of the model in describing the health of past populations.

Palaeopathological problems

Investigations of the epidemiology of infectious diseases in ancient populations are often problematical, because of unknown factors associated with the selection of material, the demography of the original population and possible alterations in disease virulence and patterns over time (Brothwell and Sandison 1967; Wood et al. 1992). In addition, various infectious diseases such as URI, lower respiratory tract infections and gastro-intestinal infections leave no signs in the skeleton. It is therefore important to find additional ways of getting more accurate information which will make statements on diseases in ancient populations more reliable.

The Greenland Eskimo skeletal material is a valuable tool for examining disease frequency in the Eskimos of the past before the European colonization of Greenland, and before the genetic admixture of the populations. The material may reveal pathogenetic or pathophysiological mechanisms in the evolution of certain diseases and provide information on the health situation in ancient times.

However, we must take care when making inferences from anthropological material, which is always selective, and probably never represents a normal population. These problems are best met by studying anthropological populations from archaeologically documented excavations. The present material from Greenland Eskimos is fairly large and well preserved, and it is assumed that the material is representative of the Eskimo adult population of ancient Greenland (Jørgensen 1953; Frøhlich 1979).

Strictly speaking, the present studies of the historical and prehistoric Eskimo samples estimate the frequency of IMED in subjects who survived to adulthood. Differences in age-specific mortality rates due to IMED-related infectious diseases in the three samples in the study (selective mortality) will therefore influence the observed frequency of IMED (Wood et al. 1992). For example, if IMED occurred in 50% of children and the mortality rate of children with IMED was 50% higher in one sample than in another, IMED frequency would be estimated as lower in the sample with the highest selective mortality rate and vice versa. A high IMED frequency could then very well indicate that the population was relatively healthy, since many survived to adulthood, while a low frequency of IMED could indicate the reverse. Information on mortality in ancient populations is therefore important when one is examining the epidemiology of diseases in the past. This information is not available at present for the prehistoric Eskimo sample, but can to some extent be found in written documents for the historical Eskimo sample (Meldorf 1907; Bertelsen 1940; Oldendov 1942; Gad 1976). These documents report high mortality rates and high morbidity in the Eskimo population from the very beginning of the colonization of Greenland. It has been proposed by archaeologists that there may have been a certain social and cultural decline in the Inuit populations in this period (McGhee 1994). This is based on findings suggesting loss of handicraft skills, linguistic and artistic competence and changes in dietary patterns due to the loss of highly specialized hunting skills. It is therefore likely that the Eskimo populations before

the colonization were healthier than after colonization while the health of the modern Greenland population has improved compared with the period from colonization until the middle of the twentieth century.

Implications of IMED results

The traces of IMED in skeletal material are left during the formation and growth of the pneumatized cell system, and can be interpreted as an indicator of general health in childhood since the disease complex includes typical childhood diseases such as RAOM and CTD as well as COM, which is a disease of childhood as well as adulthood. The frequency of IMED appeared in the present study to have increased from ancient times to more recent and modern times. This finding was emphasized by the fact that the lowest frequency of IMED was found in the isolated SE and NE regions. The above consideration of mortality rates makes it reasonable to suggest that this study showed that IMED frequency was lowest in the ancient pre-colonization period, followed by a substantial increase in IMED frequency after colonization, and a small decline in modern times. The results thus suggest that contact between the Eskimos and the Europeans formed the basis for the increase in IMED. A factor which may have been important is the introduction of specific viral and bacterial species to which the Eskimos had little or no resistance. This accords well with what we know of the spread of measles, smallpox, venereal diseases and tuberculosis etc. in several indigenous populations following contact with people from the Old World and in Third World populations in more recent times (Larsen and Milner 1994). Another important factor may have been the known changes in social, cultural and dietary habits brought about by the colonization of Greenland and the establishment of missionary stations, which led to an increase in population density (Gad 1969; McGhee 1994; Larsen and Milner 1994). Awareness of this could be useful even today, when attempts are made to establish contact with indigenous peoples or to incorporate them in the modern world.

Diachronic aspects of the pneumatized cell area

The area of the pneumatized cell system in the temporal bones of the Greenland Eskimos seems to have decreased from past to present. This tendency falls into line with the suggested increase in IMED in the same period, following a certain sequence of events: an increased frequency of URIs in childhood leads to a decrease in the pneumatized cell area and an increase in the frequency of IMED, which again leads to an increased frequency of very small or highly asymmetrical pneumatized cell areas. The influence of genetic admixture between Eskimos and Europeans is difficult to estimate, and although the examination of cranial influence on the pneumatized cell area in this study did not reveal any evidence of genetic influence, this may be a somewhat inadequate interpretation of a complex interaction. However, as the extent of genetic admixture in the historical Eskimo sample was considered low, a genetically determined difference in pneumatized cell areas between this sample and the prehistoric Eskimo sample was not expected (Frøhlich 1979). Furthermore, when we compare the median cranial dimensions of the historical Eskimo sample with those of the prehistoric Eskimo sample from the west, we can see that only the maximum breadth of the males seem to differ (see Table 4, 5 and 14). However, maximum breadth was not correlated with area. These considerations may therefore support the claim that the genetic influence on diachronic change in pneumatized area in the present study is minimal.

The appearance in terms of distributions of the pneumatized cell areas also seem to have changed with time. The modern Greenlanders, the majority of whom were born during the antibiotic era, exhibited a greater spread in area distribution than the skeletal anthropological samples (see Fig. 30 a,b,c). As proposed by Gregg and Steele (1982) this apparent diversity may be an effect of the use of antibiotics, which presumably reduce the extent of the lesions induced. This may either be due to a diminution in the virulence of the infection or to a shortening of the duration of the infection.

Conclusions

The study showed that it was possible to measure the pneumatized area of the temporal bone in anthropological skeletal material. This could be done with acceptable accuracy, repeatability and reliability. The area correlated bilaterally in all three samples, as clinical studies have also found. The area in the historical Eskimo material and the modern Greenlanders neither correlated with cranial size nor exhibited sexual dimorphism. However, in the prehistoric Eskimo material making up the largest sample, sexual dimorphism was found: males had significantly larger areas than females. In the prehistoric Eskimo sample there were also geographical differences in area, but these did not follow the regional differences in cranial morphology.

The hypothesis that IMED can be inferred from the distribution of pneumatized cell areas in anthropological skeletal samples was confirmed. This was exemplified in Greenland Eskimos and was validated by documentation from the literature, by CT scanning of crania suspected of IMED and by the examination of

modern living Greenlanders known to have had episodes of IMED in childhood, where the close association between IMED and small or highly asymmetrical pneumatized cell areas was confirmed. From this a statistical model, the polychotomous logistic regression model, was developed for the present purpose. The model incorporated the information provided by bilaterality and asymmetry, and was thus well suited to the analysis of paired organs such as the ears. A larger sample size than the 34 modern Greenlanders would have been preferred as the basis for the development of the estimation procedure, but this was not possible, mainly for ethical reasons. In spite of the rather small sample size, the significance of the results was evident in both parametric and non-parametric statistics. When the model was applied to the two anthropological samples, the secular frequency of IMED in Greenland Eskimos could be estimated. This indicated that the frequency of IMED was low in prehistoric Greenland before the colonization of Greenland in 1721 AD, and especially low in the SE and NE regions of Greenland, which are presumed to have been without European contact until lately. After the colonization of Greenland the frequency of IMED seemingly increased and probably peaked before the twentieth century, when there may have been a minor decrease. This corresponds with historical reports from the post-colonization period. Several factors introduced by colonization may have been involved in this increase in the frequency of IMED: the introduction of otherwise unknown viral or bacterial species to the Eskimo societies; the social, cultural and dietary changes; and the increase in population density which is known to have taken place. The secular differences in the areas and distribution of pneumatized cells among the three samples could be interpreted as supporting an increase in IMED frequency. Although the influence of the increasing genetic admixture of the Eskimo population and the Europeans could not be shown to be important, the complexity of this issue requires some caution in our conclusions.

The close relationship between IMED and URI, and between these diseases and poverty, makes the method well suited for evaluating the general health of past societies. Additionally, the evaluation of IMED by the method presented in this study has several advantages in a palaeopathological and a palaeoepidemiological context. First, the method is based on an unbiased evaluation of IMED in anthropological material from the pneumatized cell areas. This contrasts with previous, clearly biased methods for the evaluation of IMED based on gross inspection, examination of middle ear ossicles and subjective classification of the cell system. Secondly, the method has the advantage over other general health indicators such as cribra orbitalia, Harris's lines and dental enamel hypoplasia that the temporal bones are often preserved and abundant in skeletal assemblages. Thirdly, the method is based on modern medical research on a disease that occurs worldwide with largely equivalent clinical manifestations.

The method applied and developed in the study seems to be useful for the evaluation of the frequency of IMED in ancient populations, but is too insensitive to permit individual risk estimation. The estimated frequencies must be considered as minimum frequencies, only indicating IMED in subjects who survived to adulthood. However, the method may prove to be a valuable tool for the comparison of frequencies of IMED in different samples, provided the samples are examined in comparable standardized studies. It could be interesting to do studies of anthropological samples which have already been studied with accepted palaeopathological methods and to compare this with the results obtained using the present method. The method requires a homogeneous skeletal sample, archaeological reports as support material, X-ray apparatus, X-ray film, a desktop computer, a digitizer and a computer program for planimetrical analysis.

Summary

This study was done to examine the hypothesis that otitis media (OM) can be detected in human skeletal material. The idea was suggested by the high frequency of IMED in the modern Greenland Eskimos. The Greenland Eskimo skeletal samples housed in the Laboratory of Biological Anthropology at the Panum Institute made up the material. The aim was to develop a model for estimating the frequency of OM in historical and prehistoric Greenland Eskimo crania. This model was based on the distribution of the pneumatized cell areas of the temporal bones. Studies in the literature supported the reasoning behind this assumption, since clinical studies and animal experiments have shown a close association between hypocellular or highly asymmetrical pneumatized cell areas in the temporal bones and infectious middle ear diseases (IMED) – i.e. chronic OM, recurrent acute OM and chronic tubal dysfunction – in childhood.

Three samples were used in the study, two skeletal samples and one sample from living Greenlanders. The two skeletal samples were from before and after 1721 AD, when the European colonization of Greenland took place. A total of 183 crania from adult individuals were examined; 56 of these were post-contact and 127 pre-contact. The living subjects were 34 adult Greenlanders who were questioned about IMED in childhood. X-rays of the temporal bones were taken using the Runström II lateral projection. The pneumatized cell areas were subsequently measured in blind trials.

The results showed that it was possible to measure

the pneumatized cell areas with an acceptable accuracy, repeatability and reliability which were analysed using a variance component model. Biological variation was estimated to account for 88% of the total variation. Although the living sample was rather small, it was possible to confirm the high correlation between exposure to IMED in childhood and hypocellular or highly asymmetrical pneumatized cell areas. From this, a polychotomous logistic regression model was developed. The model included bilateral information from the two ears, including asymmetry, and was thus appropriate to studies involving paired organs. Eight (23.5%) of the living subjects were classified by the model as having had IMED. The sensitivity was 67%, the specificity was 92% and the positive predictive value was 75%. Because of the small sample size the confidence intervals were wide. The pneumatized areas differed among the samples, and before the model was applied to the two skeletal samples the data were converted into Z-scores. The model then classified six (4.7%) crania in the pre-contact Greenland Eskimo sample and ten (17.9%) crania in the post-contact Greenland Eskimo sample as having had IMED. This was compared with the frequency of 23.5% in the modern Greenlanders. IMED thus appears to have increased significantly in frequency from pre-contact to modern times. This was supported by the reduction in mean area over time. However, frequency depends on several factors such as the demography, migration and mortality of the populations. It is argued that, because of a presumed difference in selective childhood mortality, the frequency of IMED was lowest in the pre-contact period, highest in the post-contact period and intermediate in modern times. This is in line with the results of contact between indigenous peoples and Europeans elsewhere. A possible influence from the modern use of antibiotics was detected in the living sample as there was a greater spread in the distribution of cell areas.

Since IMED correlates with URIs and is associated with poverty, it is suggested that the method is valid for the examination of the health of populations of the past. The method offers several advantages over known methods for examining health in the past based on osteological material. The most important feature may be that the method can be used in blind trials. One disadvantage is that the method only accounts for IMED in individuals who survived to adulthood. The application of the method to anthropological material previously examined by other methods may further validate the usefulness of the method presented here for describing health in past populations.

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