features of drug trials whose presence or absence has been used to assess reports of trials (Ross, 1951; Mahon and Daniel, 1964; Reiffenstein *et al.*, 1968). Such a method of assessing reports may, however, give the impression that if these requirements are met then the therapeutic trial must be reliable and valid. It overlooks the fact that many other points—for example, the selection of patients, the dose, mode of administration of the drug, and method used to assess the response to treatment—can be equally important in determining the validity of a trial. Use of the check list ensures that features which may be important in assessing the report of a particular therapeutic trial will not be forgotten.

The lack of important items of description in some apparently well-designed and well-executed trials is not necessarily the fault of the authors, but may at times be due to editorial insistence that papers be short. The check list can help not only authors writing up reports, but also the editors to whom they are submitted, to ensure that all the essential information needed to assess the reports is included. It can also help the individual doctor to reach a soundly based conclusion on the validity of a report in the same way as a thorough clinical examination of a patient helps him towards a correct diagnosis.

The check list, however, should not be regarded as an

automatic device for assessing the quality of a report. Its proper use requires some familiarity with the various factors that may influence the results in a particular therapeutic situation.

The use of check lists can be extended to reports of investigations other than therapeutic trials—for example, case reports of unwanted effects of drugs, reports of retrospective studies, and reports of pharmacological investigations performed without therapeutic intent. These different classes of report require different check lists, which would, however, be similar in arrangement to the check list described in this paper.

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How Old is Leprosy?

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One by one the myths and legends surrounding leprosy are being exploded. Leprosy is incurable, said the world's leading experts gathered at the first Leprosy Congress, held in Berlin in 1897—that was the only thing they agreed about. The myth of incurability was destroyed when the sulphones came into use. Later the bacteriostatic activity against *Mycobacterium leprae* of dapson and sulphamethoxine and more recently of clofazimine and rifampicin,¹ was demonstrated experimentally in the mouse foot-pad. Again, far from being very catching, as used to be thought, leprosy is now known to be one of the least contagious of transmissible diseases.

In the same way, the antiquity of leprosy—for years almost an article of faith among doctors and laity alike—is being questioned and denied. The age of doubt began when a

Danish general practitioner, V. Møller-Christensen, started on the second phase of a distinguished career that has taken him via the ossuaries of a mediaeval churchyard in Denmark and the osteological collections in many museums to the chair of the history of medicine in the University of Copenhagen. Blessed with the flair of a sleuth-hound and the patience of Job, and encouraged by fortune's unexpected smile, Møller-Christensen lighted on the cemetery attached to a mediaeval monastery near Næstved in Denmark. Here were buried (from about A.D. 1175 to 1544) some hundreds of persons whose bony extremities exhibited the well-recognized changes noted in leprosy. Not content with recording with scrupulous care and accuracy these changes, described in the living by D. E. Paterson,² S. Karat and his colleagues,³ and others, Møller-Christensen^{4,5} noted two departures from the normal that were consistently present in skeletons showing advanced destruction of the phalanges—namely, erosion of the anterior nasal spine and of the alveolar process of the maxilla. He called this condition *facies leprosa*, or the Bergen syndrome. The previously unnoticed changes were subsequently seen radiographically in living patients suffering from severe lepromatous leprosy, and are now generally recognized as pathognomonic of leprosy.

Ritual Defilement

One of his disciples, J. G. Andersen,⁶ has recently published a doctoral thesis embodying the results of his own linguistic, osteo-archaeological, and clinical researches into the history of leprosy. He demolishes without difficulty the flimsy deductions that certain swellings referred to in the Ebers papyrus (c. 1552-1350 B.C.) were manifestations of leprosy. He goes on to confirm the view rapidly gaining acceptance that the word translated "leprosy" in the Old Testament (*tsara'ath*) does not refer to true leprosy at all, but rather to a

FIG. 1.—A senile female skeleton excavated in 1951, with flexion contractures in the hip joints, *facies leprosa*, and leprosy changes in hands and feet.

FIG. 2.—A mature female skeleton, excavated in 1951, with facies leprosa and leprosy changes in hands and feet.

state of ritual defilement of the scaly human skin and of cloth or leather or the walls of houses (*Leviticus*, chapters 13 and 14). Noting that excellent clinical descriptions of leprosy existed in India (c. 600 B.C.) and that leprosy was apparently unknown in Greece and the Western world before about 300 B.C., he concludes that the disease was probably brought to the Mediterranean littoral by the soldiers of Alexander the Great returning from the Indian campaign in 327-326 B.C. The leprosy of the New Testament (*lepra*) could not have been true leprosy, for which the Greek medical term was *elephantiasis*. Andersen reminds us that the earliest extant osteological evidence of leprosy is furnished by two Coptic mummies dated from the 5th century A.D.^{7,8} His master, Møller-Christensen, found no signs of bony abnormalities attributable to leprosy in 1,844 Egyptian skeletal remains from 600 B.C. to A.D. 600, nor in 695 skeletons from Lachish (near Jericho) dated from about 700 to 600 B.C.

FIG. 3.—A mature female skeleton, excavated in 1951, with facies leprosa and leprosy changes in hands and feet. This x-ray picture of the maxillary bone shows maximal atrophy of the maxillary alveolar process, though with the teeth still in situ.

With a wealth of quotations from Greek and Latin authors, Andersen traces the clinical entity we now call leprosy through the fascinating verbal vicissitudes to which it has been subjected down the ages. After a peep into Arabic, mediaeval, and Scandinavian literature he comes to the bones of the matter, if the expression be allowed. Studying the skeletal remains found in the mediaeval churchyard at Næstved and first investigated by Møller-Christensen, Andersen scrutinized bones from some 207 individuals, giving age- and sex-groups, and detected undoubted signs of leprosy in the skull and signs suggestive of it in the extremities. When the latter lesions are symmetrical and multiple,

the diagnosis of long-standing lepromatous leprosy with widespread peripheral neuropathy becomes likely. The rhino-maxillary changes, and the specific and non-specific destruction of phalanges of hands and feet and of the mid-tarsal bones, are then described and appraised. The dry bones of these anonymous sufferers from leprosy, living and dying in their mediaeval obscurity, are made to live again as Andersen decks them out with the flesh and blood of their living counterparts in West Bengal today.

Lepromatous Disease

One interesting fact to emerge is that the bony changes seen in the mediaeval material are almost exclusively those that are due to leprosy of the multibacillary, low-resistant, or lepromatous type, which is the predominant type among light-skinned Caucasians today. Evidence of high-resistant leprosy (tuberculoid) appears to be virtually absent from these skeletons, and it is only questionably referred to in mediaeval literature. Further, the bony remains are indicative of leprosy, and of leprosy alone. Whatever may be said of the wide lay connotation of the word "leprosy" in the England of the Middle Ages⁹ and of its extension to non-leprosy skin conditions such as mange and mildew—in mediaeval Denmark at least, "leprosy was well and truly diagnosed" as Andersen justly remarks. Of other diseases, in particular syphilis and tuberculosis, there is no evidence in these bones, just as there is none in the Trentholme Drive remains.¹⁰

Andersen's study is not the only one to come from Møller-Christensen's disciples. K. Danielsen¹¹ has described disturbances in the odontogenesis of the maxillary incisors in skeletons of children who had suffered during life from low-resistant leprosy. P. Sager¹² has put not only osteo-archaeologists but also orthopaedists and rheumatologists in his debt by elucidating the pattern of cervical spondylosis in mediaeval skeletons from the same Danish churchyard. The publication of this work is opportune, coinciding as it does with the use of the newer techniques of fluorescent microscopy and microradiology of non-decalcified sections in the investigation of bones obtained at operation from patients with leprosy.¹³

Almost a century ago, another Scandinavian, Hansen, was puzzling over some microscopic, brown, rod-shaped bodies he found in leprosy lesions, and thus peered into the unknown future of the science of bacteriology and the pathogenesis of leprosy. Today Andersen the Dane peeps into the fascinating past of leprosy, and by painstaking observation of dry bones and living patients helps towards a deeper understanding of this remarkable disease.

The three illustrations are reproduced by permission from *Ten Lepers from Næstved in Denmark* by Vilhelm Møller-Christensen, M.D. (Copenhagen, Danish Science Press, 1953).

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