RHINOSCLEROMA*

By E. ZWIEFACH (London)

In the history of the disease three dates are important. In 1870 the disease was first described by Hebra. In 1876 Von Mikulicz described the histology and the characteristic foam cells which since bear his name. In 1882 Von Frisch discovered the Bacillus scleromatis.

Hebra described the disease as rhinoscleroma. In 1932 the International Congress of Otorhinolaryngology changed the name to scleroma, emphasizing that the disease attacks not only the nose but other parts of the respiratory tract as well. Many authors still call it rhinoscleroma, to stress that the primary site is the nasal cavity.

Geographical Distribution

The disease occurs sporadically all over the world, and endemically in the following countries: Russia, Poland, Hungary, Egypt, Central America (e.g. Mexico, Guatemala, Salvador, Honduras), Indonesia. There is no racial or climatic similarity between these countries, but in the areas where the disease is endemic, poor hygienic conditions are invariably the rule. It is well known that the disease affects the "great unwashed", at least during the incubation period which may be very long.

But this is not the only explanation of the geographical distribution. For example in Guatemala rhinoscleroma is endemic in the south-east, but is practically unknown in the north-west, in spite of the fact that the population does not differ racially or hygienically. In Russia the Ukraine is the centre of disease; in Poland the eastern regions are most affected. In Italy most cases come from the regions near Florence and Bologna, although southern Italy is much poorer. No satisfactory explanation can be given. The highest known incidence of the disease is in eastern Poland: Jurasz (Lwow) saw an average of two cases a week.

Ætiology

There are two views: firstly that the disease is caused by Frisch's bacillus, secondly that it is caused by a filtrable virus and that the bacillus is only present as a secondary invader.

There is a great likelihood that the bacillus is the causative organism

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as it is almost always present in the disease and produces antibodies in infected persons. It disappears with treatment, together with the signs of the disease. Moreover, sensitivity tests on the bacillus recovered from a patient may serve as a useful guide for the antibiotic treatment of the disease.

It is true that only two out of three of Koch's postulates are fulfilled: the bacillus is always present in the lesions and it can be cultured, but the disease cannot be reproduced experimentally in animals. Equally all human experiments on volunteers, such as injecting the bacilli into the concha, and placing a piece of cotton wool soaked in a culture in the nose, proved negative.

It is well known that animals are immune to the bacillus, and in human beings a very long exposure is needed, a positive result of experiments, therefore, would have solved the question, but negative results do not rule out the bacillus as the causative organism. That a filterable virus is the cause, is a hypothesis in support of which no one has produced any evidence.

The disease is contagious and many authors have reported several cases occurring in the same family. In Celebes, Indonesia, scleroma is very common. Oomen (1952) examined one village with 1,100 inhabitants: 2 per cent. had scleroma, most of which were relatives. He regards prolonged house-relationship as the decisive factor. The disease occurs in all age groups and in both sexes.

Bacteriology

The Frisch bacillus, is a Gram-negative encapsulated rod, is frequently referred to as Bacillus scleromatis or Klebsiella scleromatis. The Klebsiella group also includes Friedlander's bacillus and bacillus ozœnae. There is here another controversial point whether or not the Frisch bacillus can be distinguished from other bacilli of the group, e.g. Friedlander's bacillus. Morphologically and on culture the bacilli may be identical, but according to Levine and Hoyt (1948) and Kauffmann (1949), they differ in their biochemical reactions.

All Frisch bacilli recovered from scleroma cases gave a characteristic biochemical pattern and in 532 cultures from persons with or without disease of the ear, nose and throat, other than rhinoscleroma, the results were negative (Levine, 1951).

Serological Tests

Antibodies are present in the serum of scleroma patients, and 80 per cent. of patients gave a positive complement fixation test (H. Streit 1928). Levine and Hoyt (1948) have examined the sera of 12 scleroma patients. All were strongly positive, whereas only 15 out of 534 sera patients with other assorted diseases gave a positive reaction, none so

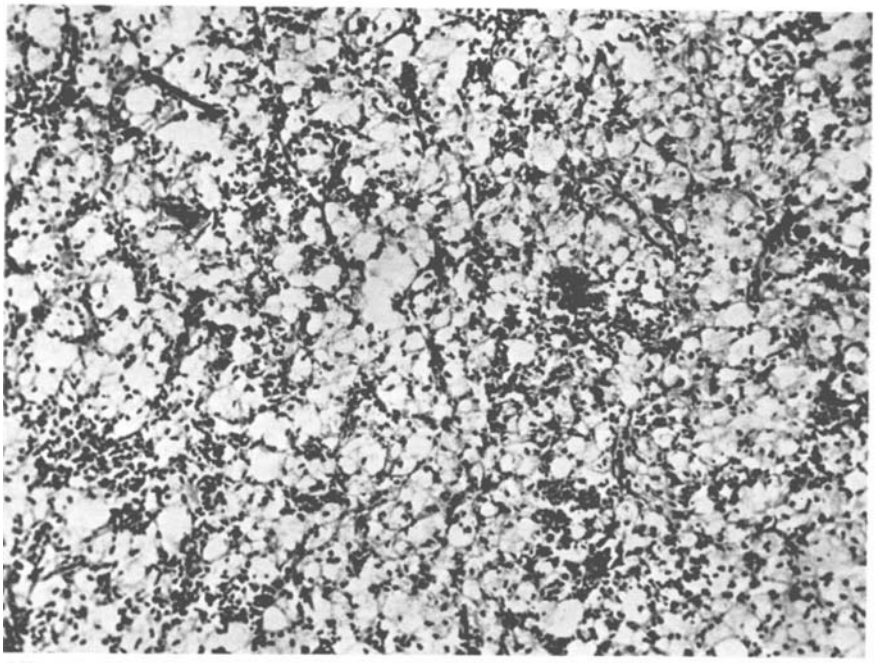
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strong as in scleroma patients. These authors suggested that a strongly positive test may be considered as reliable.

Histopathology

The disease has three histological stages:

(1) *In the first stage* there are signs of chronic inflammation with small round-celled infiltration in the subepithelial tissue. Plasma cells are numerous. The bacilli may be seen in the tissue spaces.



Microphotograph of slide of the patient Mrs. P. S. described at the end of this paper. Nasal biopsy showing characteristic histological picture of rhinoscleroma. Note large number of Mikulicz cells.

(2) *In the next stage* phagocytosis takes place and bacilli are seen in the cells; these enlarge and become vacuolated to form a typical Mikulicz (foam) cell. The Mikulicz cell is probably the result of a non-specific reaction to toxins of Klebsiella type bacilli. The parent cell may be any cell, even epithelial. Later the cells degenerate and hyaline and Russell's bodies are seen; these probably represent the ultimate fate of the Mikulicz cells (Ellis, 1952). They are, however, not specific for scleroma as similar structures can frequently be seen in sections of simple or allergic nasal polypi or in the infected nasal mucosa (I. Friedmann, 1954).

(3) *In the third stage* fibrous tissue invades the typical scleroma tissue

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and may partially or completely replace it. Mikulicz cells and hyaline bodies may be scanty or absent.

Morbid Anatomy

As in the histology we recognize three stages, but overlapping is frequent:

(1) *Catarrhal or rhinitis stage* produces a picture of atrophic rhinitis with fœtid crusts. The nasal cavity may not be widened and the mucosa may be infiltrated.

(2) *Granulomatous stage.* Small tubercles appear in the mucosa resembling lupus but harder. The tubercles enlarge, coalesce and form irregular large masses. The colour is first reddish brown, later pale. The masses may be covered with crusts. In this stage the swellings may not be very hard; they may bleed easily. Deep ulceration is rare, but superficial traumatic erosion is not infrequent.

(3) *Fibrous or nodular stage.* This is reached after several years duration. The contraction caused by fibrous tissue is irregular; the surface, therefore, becomes nodular and very hard, hence the name of the disease. It should be clear that the fibrous stage means that the disease has reached its peak and from then on a relative regression can be expected (Quevedo, 1949).

Site. The primary site of scleroma is almost always the nasal cavity. It usually begins on the anterior part of the septum, floor or turbinates. From there it extends backwards into the post-nasal space, pharynx, larynx, trachea and bronchi; forward into the upper lip and laterally into the sinuses. The superior meatus and olfactory cleft are free. *Primary* laryngoscleroma occurs rarely if ever.

Clinical Picture

Nose. The disease begins with symptoms and signs of atrophic rhinitis. Sense of smell is usually preserved as the olfactory cleft is not involved. Later, progressive nasal obstruction is complained of. In patients showing external deformity this may be due to masses pressing from inside or to invasion of the external nose and lip by the process.

Post-nasal space. The sites of predilection are the posterior end of the septum, which may be greatly thickened, and the eustachian cushions. Anæsthesia is frequently the first sign of invasion of the soft palate and is very characteristic. In the fibrotic stage the soft palate is pulled upwards, and the fairly characteristic picture of the so-called "gothic palate" is produced. The uvula disappears or may be drawn into post-nasal space.

Pharynx. Here the pillars are invaded and become fibrotic, pulling the base of the tongue up. The changes are frequently symmetrical. The

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entrance to the post-nasal space may be very narrow, but is not obliterated.

Larynx. Laryngitis sicca frequently precedes the granular stage. In the latter the lesion is first seen in the sub-glottic region and it may remain there for a long time, or it may spread early into other parts. At the beginning the swelling is usually symmetrical and on the lateral walls. From the sub-glottic region it may spread upwards and involve the cords and posterior surface of the epiglottis, which is another characteristic site. In some cases the swelling may become irregular, assuming various shapes and sometimes resembling multiple papillomata. The disease may extend into the trachea and bronchi.

Summing up the clinical picture it should be emphasized that rhinoscleroma does not follow any rules, and no description of the disease can be complete. Some cases are very benign and of limited extension; others show marked invasion with tremendous deformities; and between these two extremes we find the most varied range of possibilities.

Diagnosis

Diagnosis of rhinoscleroma can be very easy or very difficult. It is easy to diagnose in a locality where it is endemic, or in the later stages of the disease. It may be very difficult, however, for the rhinologist who has never seen a case before.

The diagnosis is based on the following evidence:

(1) *History* including periods of time spent in endemic areas.
(2) *Clinical appearance.*
(3) *Histology.*
(4) *Bacteriology.*
(5) *Serology.*

Some authors include skin tests, too.

In the first stage of the disease when there is ozœna the diagnosis may be very difficult indeed, as the biopsy may be negative. Many cases of ozœna have been diagnosed and treated which later proved to be scleroma. Wexler (1949) in America re-examined 27 cases of ozœna and seven of these were found to have a culture and biopsy positive for scleroma; most of them were Mexicans. It is important that each case of ozœna coming from an endemic region should be examined for scleroma.

In the second stage the clinical picture and biopsy are the most important. In the slide we look for three features; Mikulicz cells, hyaline bodies, and Frisch bacilli. The first two are not as explained above pathognomonic for the disease as they are found in many other chronic inflammatory processes and in tumours; in scleroma, however, they are present in great numbers. Some authors regard Mikulicz cells loaded with bacilli as pathognomonic.

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In the third stage again the biopsy may be negative and we have to rely on the same features as in the first stage.

Differential Diagnosis

In the first stage, ozœna, syphilitic atrophic rhinitis, and lupus may give a similar picture.

Later a typical picture with very hard swellings in the nose, post-nasal space and larynx is so characteristic that it can hardly be confused. The less obvious case will have to be differentiated from any ulcerative and non-ulcerative lesions of these regions. Ultimately the diagnosis rests on the biopsy, culture and serological tests.

Prognosis

The disease extends over many years. Spontaneous cures are rare, but remissions and relapses are very common. The patients die not from the disease, but from respiratory obstruction or intercurrent infection. The prognosis is very poor in cases where the lower part of the trachea and bronchi are involved (5-10 per cent. of cases).

Treatment

It can be said that almost every chemical product and almost every surgical procedure has been tried, but most of them are of historical interest only. X-rays and radium were used in pre-antibiotic days. It usually led to a temporary arrest of the disease due probably to fibrosis. Dosage was about 2,000 r.

Present treatment is conservative and/or surgical.

(1) Conservative

(*a*) *Antibiotics*. The disease responds well to some antibiotics. The antibiotic most frequently used is streptomycin. Other effective antibiotics are aureomycin, terramycin and chloromycetin. The disease does not respond to penicillin or sulphonamides. Sensitivity tests should be carried out prior to treatment with antibiotics.

(2) Surgical

Tracheotomy is the main surgical procedure when there is respiratory obstruction. Other surgery is as a rule contra-indicated during the evolution of rhinoscleroma. In the fibrotic stage plastic surgery may be required. Before any plastic surgery of the larynx is performed laryngeal dilators should be tried first. It should be remembered that the laryngeal cartilages may become soft and pliable (Quevedo, 1949). Laryngo-fissure with excision of the scars and skin grafting may lead to collapse of the larynx. The plastic procedure is, therefore, only justifiable after dilatation has failed.

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TABLE I.

RESULTS OF TREATMENT WITH ANTIBIOTICS

Author	Antibiotic and No. of cases	Dosage in gm.	Cure	Failure	Follow up	Further treatment	Cure	Failure	Follow up
	Streptomycin								
A. H. Miller	3	28–30	4	0	2–3 years				
S. V. Mikhailovskii	12	9	doubtful*		?	streptomycin 7 gm.	12	0	?
N. P. Kniga, A. A. Shvartzberg	29	6–20	29	0					
A. Del Magro and V. Mattioli ..	10	12–60	9	1†	4 years	streptomycin	1	0	?
P. L. Ćurković	3	35–45	3	0	6 months				
A. R. Hollender and H. M. Scheer	2	36	2	0	1–2½ years				
El-Hakeem *et al.*	2	44	0	2	?	aureomycin 20 gm.	2	0	?
	Chloromycetin								
P. L. R. Maggi	1	76	1	0	?				
El-Hakeem *et al.*	1	24	0	1	1½ months	aureomycin 20 gm.	1	0	?
	Terramycin								
H. Waeser	1	48	1	0	?				
R. Blaubaum, N. Asherson‡ ..	1	two courses	0	1	?	aureomycin	great improvement		
	Aureomycin								
El-Hakeem *et al.*	2	20	2	0	?				

* In this series the bacilli re-appeared without the signs of the disease after 1–2 months. Another course of streptomycin was given and the bacillus disappeared again.

† This case had 12 gm. of streptomycin only and the disease recurred after 3 years. A second course of streptomycin was given with cure.

‡ This case is described at the end of this paper. Although these cases are regarded as cured by most of the authors, the outcome is still in doubt as the follow up was either not given or was too short and there is still a possibility of recurrence which in rhinoscleroma is so common

Cases Observed in Poland

The author has seen cases of scleroma in 1939 and 1940 in the eastern part of Poland which, as explained before, is an endemic region.

The cases seen can be divided into two groups:

(1) *Long-standing cases* treated mainly in Lwow which was a scleroma centre. These cases came for regular check and they were eight in number. All were in the late fibrotic stage, all had hard nodular masses in the nose. One of them had almost complete nasal obstruction with external deformity.

In the post-nasal space there was a varied degree of fibrosis and stenosis. All had some changes in the soft palate—scarring or high gothic palate. Five had laryngo-scleroma; in one case the larynx was completely stenosed and he had a permanent tracheostomy.

Treatment. All had deep X-rays with improvement; some had vaccino-therapy without improvement; two had periodical dilatation of the larynx; and one did the dilatation himself. In no case was bronchial extension diagnosed.

(2) *New cases* seen were six in number. Four presented because of respiratory obstruction, dyspnœa, and various degrees of stridor. Two complained of nasal symptoms, one of nasal obstruction and another of obstruction plus external deformity.

On examination of the nose two had atrophic rhinitis only; four had firm irregular swellings of greyish-bluish-red colour partly covered with crusts. The changes were mainly on the septum and turbinates.

Examination of the post-nasal space revealed thickened posterior ends of the septum in most cases; some had swellings around the eustachian tubes; one had a swelling in the roof resembling adenoids but harder. In one or two cases the soft palate was infiltrated.

The pharynx was mainly dry.

The larynx was involved in four cases, and all of them had more or less symmetrical narrowings of the sub-glottic region. In two patients the cords were involved. One had swelling of the epiglottis.

Diagnosis was made in two patients in consultation with a local ear, nose and throat surgeon, on the clinical appearance and bacteriology only. A histo-pathologist was not available. The other four patients were diagnosed histologically as well.

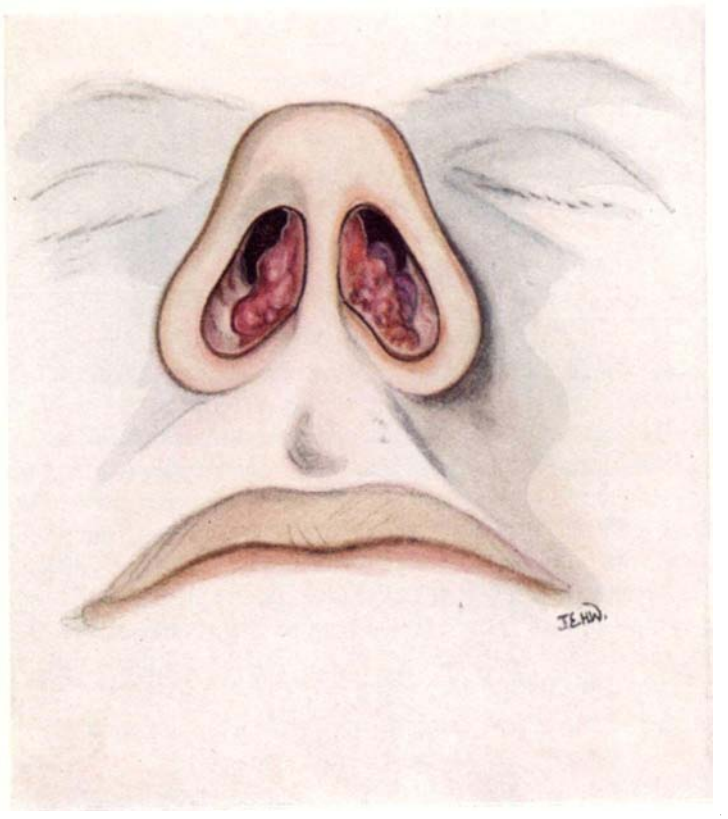
All new patients were treated with deep X-rays, most of which improved, but the follow-up too short to be more precise. In one case an urgent tracheostomy was performed.

Case Seen in London

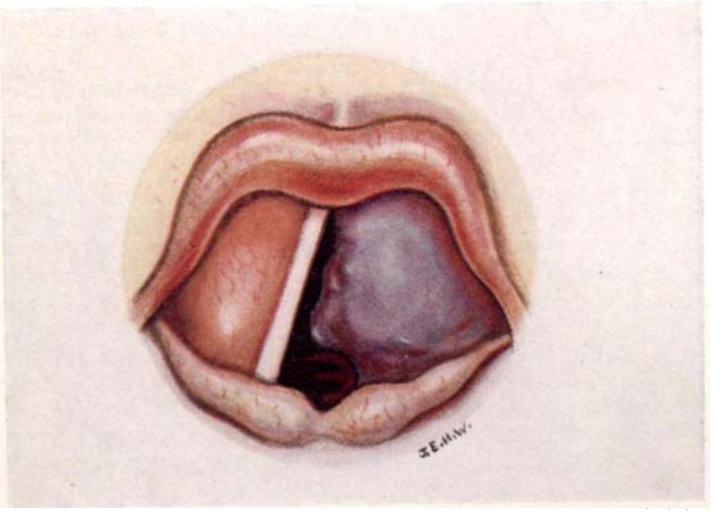
A woman, P.S., aged 56, was sent in July, 1954, to Mr. N. Asherson by Dr. Blaubaum of Melbourne, Australia, with the following history:

In 1942 she developed a swelling in the subglottic region with respiratory obstruction. Bronchoscopy was performed, biopsy taken, causing profuse hæmorrhage. A diagnosis of rhinoscleroma was made. She was

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Rhinoscleromatous changes in the nose.



Changes in the larynx in the same case.
There was also a sub-glottic stenosis not shown in the picture.

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treated with deep X-rays with great improvement and was well until 1950 when a tracheal stenosis appeared, the lumen of which was only 3 mm. wide. She was again treated with deep X-rays, this time without improvement, but tracheal dilatation provided her with an adequate airway. In 1953 she was given two courses of terramycin which had no effect.

In July, 1954, the patient was seen at the Royal National Throat, Nose and Ear Hospital, and the findings are shown in the pictures.

In the last few months she was treated with aureomycin, apparently with great improvement.

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REFERENCES

Ćurković, M. (1950) *Arch. Otolaryng. (Chicago)*, **52,** 253.
Del Magro, A., and Mattioli, V. (1953) *Boll. Mal. Orecch.*, **71,** 307.
El-Hakeem, A., El-Samma, E., and Mossallam, I. (1954) *J. Laryng.*, **68,** 523.
Ellis, M. (1952) Rhinoscleroma. *In British Encyclopædia of Medical Practice*, 2nd edition. London, Vol. **11,** p. 12.
Friedmann, I. (1954) Personal communication.
Hollender, A. R., and Scheer, H. M. (1954) *J. int. Coll. Surg.*, **21,** 24.
Hoover, W. B., and King, G. D. (1953) *Arch. Otolaryng. (Chicago)*, **57,** 79.
Jurasz (1912) Über das Sklerom. *Der Amtsarzt*, No. 8. Quoted by Streit.
Kauffmann, F. (1949) *Acta path. microbiol. scand.*, **26,** 381.
Kniga, N. P. (1952) *Vestn. Oto-rino-laring.*, **14,** 63.
Levine, M. G. (1951) *Amer. J. clin. Path.*, **21,** 546.
Levine, M. G., and Hoyt, R. E. (1948) *Arch. Otolaryng. (Chicago)*, **47,** 438.
Lewenfisz, H. (1949) *Przegl. lek.*, **5,** 730.
Mikhailovskii, S. V. (1950) *Vestn. Oto-rino-laring.*, **12,** 21.
Miller, A. H. (1949) *Laryngoscope (St. Louis)*, **59,** 506.
Oomen, H. A. P. C. (1952) *Docum. Med. geog. trop.*, **4,** 124.
Quevedo, J. (1949) *Ann. Otol. (St. Louis)*, **58,** 613.
Remaggi, P. L. (1950) *Boll. Soc. med.-chir. Modena*, **50,** 252.
Reyes, E. (1946) *Arch. Derm. Syph. (Chicago)*, **54,** 531.
Russell, D. A., Moore, J. M., and Mattman, L. H. (1952) *J. Amer. med. Ass.*, **148,** 642.
Shvartsberg, A., and Kozitskaia, K. N. (1952) *Vestn. Oto-rino-laring.*, **15,** 44.
Streit, H. (1928) Das Sklerom. In Denker and Kahler's Handbuch der Hals-Nasen-Ohren-Heilkunde, Berlin, Vol. 4, p. 348.
Waeser, H., and Schmidtmann, M. (1952) *Z. Laryng. Rhinol. Otol.*, **31,** 295.
Wexler, M. R. (1949) *Laryngscope (St. Louis)*, **59,** 1026.

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