SCLEROMA

REPORT OF TWO CASES

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THE first description of rhinoscleroma as a clinical entity was given by von Hebra in 1870. He considered it to be a form of cutaneous neoplasm but his assistant, Geber, suggested later that the disease was a specific chronic inflammatory process of unknown ætiology. In 1876 Mikulicz described the foam cells which bear his name and von Frisch isolated a Gram-negative encapsulated diplobacillus from the lesions in 1882. He claimed that this was the causal organism of the disease but this claim was not widely accepted. In recent years more evidence has been brought forward in support of von Frisch's view but there are still some investigators who regard the bacillus as a secondary invader rather than the primary cause. The disease was first thought to be confined to the nose but later it was realized that the pharynx, larynx, trachea and bronchi could also be affected, so it was recommended at the Second International Congress of Otorhinolaryngology in 1932 that the more inclusive name " scleroma " be adopted.

Scleroma is very seldom encountered in Great Britain and its occurrence in two Polish soldiers stationed in this country seems worth reporting. It is possible that with the influx of European refugees during the past ten to fifteen years more cases might occur. It is interesting to note that Guerrier[1] reports the disease in a Frenchman who, he suggests, contracted it from some Poles with whom he had been working for several years.

Distribution

Scleroma occurs endemically in certain areas, both in the old world and the new, and most of the cases encountered in other regions have originally come from one of these areas. The main centre of the disease in Europe is the valley of the River Pripet, a tributary of the Dnieper.[2] This area used to be a part of Poland but has now been included in the U.S.S.R. From this centre scleroma has spread to other states of the U.S.S.R., Poland, Czechoslovakia and Yugoslavia and many cases have been reported in these countries. It appears to be on the increase in Germany, Italy and Hungary. In America it is endemic in El Salvadore, the central states of Mexico and the south-eastern states of Guatemala. The island of Sumatra seems to be another main centre of the disease. Cases have arisen, however, in the native-born of most countries of the

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world. Lucas and Negus have described the case of a young woman who had never left England[3]. Cunning and Guerry[4] surveyed all the cases that had been reported in the U.S.A. and Canada up to 1942 and found that 16 out of a total of 102 patients were native-born. Since then Olson[5] states that 11 more cases have been reported of which 7 were natives of the U.S.A.

Ætiology

All authors except Quevedo[6] report that the disease attacks women rather more frequently than men. It most commonly begins between the ages of 15 and 30 but no age group is immune. It is not hereditary. Most authors agree that it is slightly contagious, basing this conclusion on the fact that two or more cases occurring in one family is not unusual. Hara *et alia*[7] have recently recorded 7 cases in one Mexican family. Proof of contagiousness is difficult, because of the insidious onset and slow progress of the disease. Most of the cases have been found in poor peasants living in filthy and unhygienic circumstances, but town dwellers and people of clean habits are occasionally affected.

Von Frisch's bacillus (Klebsiella rhinoscleromatis) can be grown from all cases and there still appears to be some doubt as to whether this organism is the cause of the disease. It is difficult to distinguish it from the Friedländer bacillus and other members of the group and it is said that it can be found in normal noses and throats as well as in other nasal diseases. Some of the confusion, no doubt, has been caused by the lack of suitable distinguishing tests between the organisms of the Klebsiella group, but recently Levine, Hoyt and Peterson,[8] following up the work of Figi and Thompson and Morris and Julianelle on the fermentation of sugars, claim that the following cultural pattern, which was derived from the study of eleven strains, is given by no other Gram-negative bacillus :

Lactose	Dextrose	Maltose	Mannite	Sucrose	Indole	Nitrate Reduction
—	Acid	Acid	Acid	Acid or —	—	+

This pattern, with the appearance of the large coalescing colonies on blood agar or nutrient agar, is sufficient to distinguish the organism from others of the group. Using this method of identification they failed to find K. rhinoscleromatis in the nose and throats of 204 normal persons and in 63 cases which had nasal disease other than scleroma.[9] It will be seen that the organism isolated from our second case gave exactly these reactions. Unfortunately, no organism was grown from the first case. That this organism is invariably found in scleroma, but not in other diseases, strongly suggests that it is the causal agent. Complement tests have been developed and may be useful in the diagnosis of early scleroma, but their value has not yet been properly assessed. It has never been

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Fig. 1.

Scleroma: Low power (× 96). Many Mikulicz cells and scattered Russell bodies can be seen.

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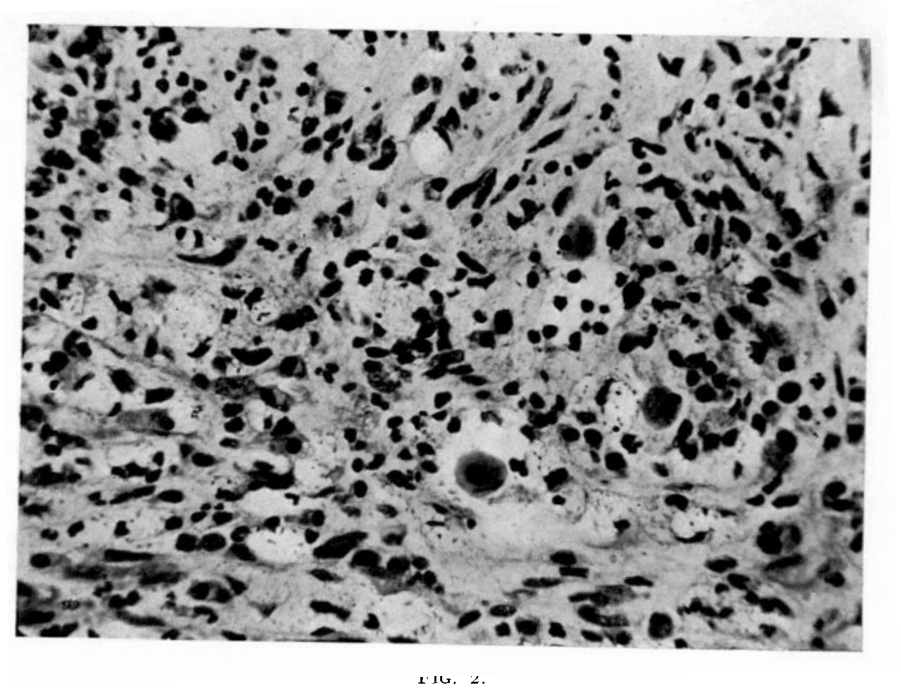


FIG. 2.

Scleroma: High power (× 415). The Russell bodies stand out clearly but the numerous Mikulicz cells are less distinct.

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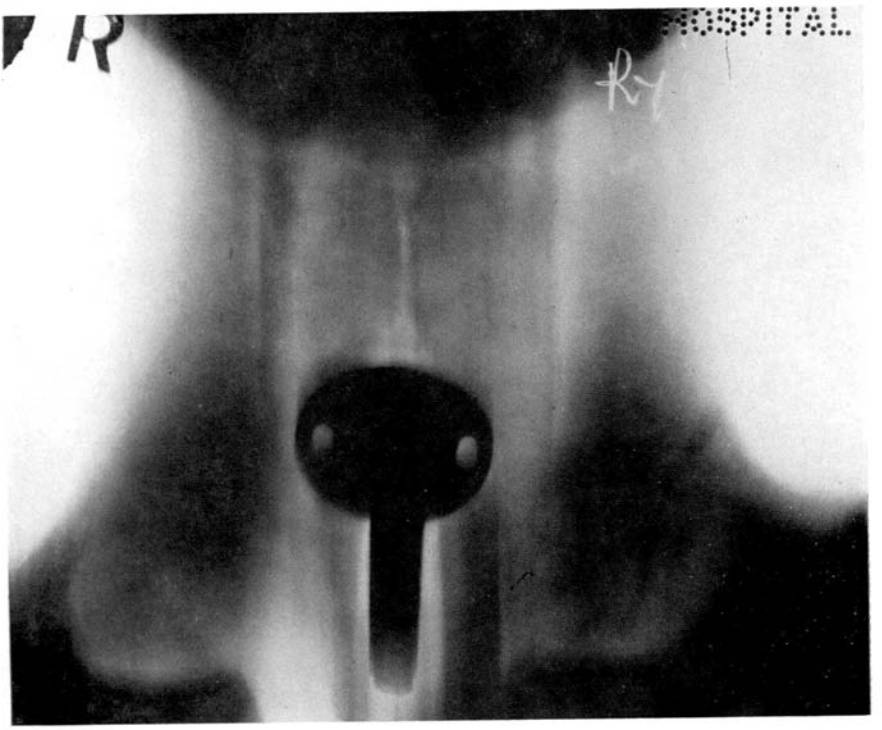


FIG. 3.

Tomograph of larynx. The airway and the ventricles have been almost entirely obliterated by swelling of the ventricular bands.

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possible to reproduce the disease by animal inoculation and some authors (Reyes,[10] Quevedo,[6] Cunning and Guerry[4]) still look upon the bacillus as a secondary invader and suggest that the real cause is a virus infection.

Pathology

The tissues become invaded by masses of inflammatory cells in which plasma cells predominate. In the first stage there is nothing diagnostic in the histology, but during the second stage Mikulicz cells and Russell bodies begin to appear. The Mikulicz cells are large cells in which the nucleus is surrounded by foamy cytoplasm. The Russell bodies are smaller, stain intensely with eosin and if a nucleus is present it is usually eccentric. The Russell bodies are degenerated plasmocytes and the Mikulicz cells are probably degenerated reticulo-endothelial cells. K. rhinoscleromatis can be demonstrated in sections of scleromatous tissue and may often be seen in the Mikulicz cells. Neither the Mikulicz cell nor the Russell body is diagnostic of scleroma because they may be found also in leprosy, bubonic plague and infective granulomas, but the combination of both with the von Frisch bacillus may be taken as diagnostic. The epithelium covering the lesion may be atrophic or hyperplastic. In the later stages there is fibrosis and perivascular infiltration and obliteration of blood vessels. The lymph glands are not involved and the blood picture is unaltered.

Clinical Description

Scleroma starts in the anterior part of the nose and gradually makes its way backwards to the nasopharynx. During the second stage it may pass forward into the upper lip and produce external deformity. The pharynx may be invaded but usually the disease misses this area and invades the larynx and sometimes the trachea and bronchi. The onset is insidious and the course and severity very variable. It often remains confined to the nose and, rarely, may even undergo spontaneous arrest. Other cases progress more rapidly and produce severe deformity—the illustrations in the articles by Reyes[10] and Quevedo[6] give a good idea of the appalling disfigurement that can occur. Even in less severe cases the nasal passages and the larynx may become completely obstructed. There is no pain, pyrexia or general constitutional effect, apart from what is produced by secondary infection and the results of obstruction in the respiratory passages. Otitis media is common. The end usually comes from some intercurrent infection after the disease has been present for years.

It is usual to divide the clinical course in the nose into three stages, but these are by no means clear-cut and all three stages may be seen simultaneously.

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Stage I : Rhinitis. The disease is bi-lateral and causes nasal discharge and slight obstruction. The appearance resembles atrophic rhinitis in that crusts form, but instead of atrophy the mucosa is, as a rule, congested, with consequent narrowing of the airway. Cases are rarely seen or, at any rate, diagnosed in this stage.

Stage II : Infiltration. The discharge, obstruction and scabbing increase and external deformities start to occur. Masses of granulomatous tissue infiltrate beneath the nasal mucosa and beneath the skin of the columella and upper lip. Similar swellings may occur in the naso-pharynx and anæsthesia of the soft palate is frequent. There is little tendency to ulcerate and bone and cartilage are not involved, though they may be thinned or displaced. The nasal cavities are usually filled with crusts and festooned with muco-pus.

Stage III : Nodular. After many years the deformity ceases to increase, and the lesions become hard and nodular from the formation and contraction of scar tissue. Complete obstruction to the nostrils may develop.

Primary laryngeal scleroma is rare but secondary involvement is common and usually appears during the second stage of the nasal disease. Extension downwards to the trachea and bronchi occurs more rarely. The sub-glottic region is most frequently attacked and the granulomatous infiltration gives rise to smooth red swellings below the vocal cords which become partially fixed. The true and false cords may also be involved and swellings occur in the inter-arytenoid region. There is less crusting in the larynx than the nose. The symptoms are increasing hoarseness, dyspnœa and cough, with the expectoration of blood-stained sputum and crusts. Many of the cases need tracheostomy.

In the pharynx the posterior wall and the posterior pillars of the fauces may be involved. The soft palate is thickened and retracted upwards and the uvula may disappear. As already pointed out anæsthesia of the palate occurs often and is an important diagnostic sign.

Diagnosis

The diagnosis has to be made from nasal diphtheria, syphilis, tuberculosis, atrophic rhinitis, leprosy, lupus, etc. In the early stages there is no characteristic clinical appearance and diagnosis depends on the histological appearance of the lesion and the isolation of K. rhinoscleromatis. Biopsy from the nose is more likely to be helpful than from the larynx. The complement fixation test may be useful. The diagnosis of more advanced cases is usually easy in areas where the disease is endemic, but when isolated cases occur in countries where the disease is rare the diagnosis may be missed unless some clue, such as the nationality of the patient, brings the possibility of scleroma to mind.

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Treatment

The number of remedies that have been tried is an indication of how resistant scleroma has been to treatment, and, up to the introduction of streptomycin, only irradiation with either deep X-rays or radium has proved to be of any real value. Small doses are used and the treatment is repeated when necessary.[11] As a rule radiation is only palliative but the disease may be kept under control for long periods and in early cases cures have been claimed by some authorities.

Penicillin and sulphonamides have no effect on the course of the disease. Some temporary improvement may occur while the drugs are being given but this appears to be due to the control of secondary infection and the condition soon relapses when treatment is stopped.[4, 6]

Streptomycin inhibits *in vitro* the growth of organisms of the Klebsiella genus, and although it is not universally accepted that the K. rhinoscleromatis is the causal agent, the trial of streptomycin in scleroma was clearly indicated. Several cases have been reported since 1947 and it is generally agreed that streptomycin is the most effective treatment so far available. New *et alia*[12] reported a case as apparently cured by streptomycin, but other authors are more cautious about claiming complete cures. Julio Quevedo in his review of scleroma in 1949[6] had treated 12 cases with streptomycin and made the preliminary report that " Although streptomycin is not the definite answer to the challenge of the disease it is to date the best weapon that can be used against scleroma ". However, he had some difficulty in getting sufficient quantities of streptomycin and does not state what dose was used. The amounts of streptomycin that have been used vary from 10 gm.[8] to about 350 gm. spread over 9 months.[13] In this latter case Cunning states that the only effect was on the secondary invaders and the scleromatous lesions looked the same as before treatment started. 1 to 2 gm. of streptomycin per day is the usual dose rate but there is no agreement yet as to the optimum dose and each case has to be judged by its progress. Additional streptomycin may be given by aerosol inhalations or penicillin may be given by this method to deal with secondary infections. Improvement begins to be noticed within two or three days of starting treatment and the organism rapidly disappears from the secretions and biopsy materials. The various toxic manifestations of streptomycin may occur during treatment and should be dealt with as they arise. In Cunning's case which failed to improve, it may have been that the organism was insensitive to streptomycin and sensitivity tests should always be done first. Miller,[14] in his study of three cases treated with streptomycin, reports that the improvement in the nose was not so great or so lasting as in the larynx and this was also our experience in our first patient. In these cases the disease had probably been present for a good deal longer in the nose than the larynx and consequently it is likely that a greater

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degree of fibrosis and vascular obliteration had occurred there, rendering the spread of streptomycin through the tissues more difficult. Even though the disease is arrested or cured, the nasal crusting and obstruction may persist if much metaplasia of the epithelium and atrophy of the mucous glands had occurred before treatment was started. When the disease is completely controlled plastic operations to restore the airway in the nose or larynx may be necessary.

Case Reports

CASE I. K. R. Male, aged 23.

This man was born in Baranowicz, in North-East Poland, in 1924, and lived there until 1939 when he was taken to Russia as a prisoner. He escaped in 1941 and joined the Polish Army. He was stationed in the Middle East in 1942 and 1943 and returned to the U.K. in 1944 where he has remained since.

In 1942, while in the Middle East, he noticed some lassitude and some scabbing of his nose and had occasional epistaxes. He also had some difficulty in breathing and intermittent hoarseness with occasional headaches. His tonsils were removed in Palestine. When he returned to the U.K. in 1944 his symptoms almost disappeared but they returned at the end of 1945 and slowly increased in severity.

In 1946 he had a nasal operation in Edinburgh and in February, 1947, he lost his voice and was treated with penicillin without benefit. In July, 1947, he was admitted to No. 3 Polish Hospital and in September had to have a tracheostomy on account of increasing dyspnœa. A biopsy was taken from the nose in October and showed typical scleromatous tissue.

He was admitted to Mount Vernon Hospital in November, 1947, wearing a tracheostomy tube and in good general condition. In the nose, the airway was narrowed by mucosal swelling and there was ulceration and crusting with a good deal of muco-pus present. In the nasopharynx there was a lot of crusting and a pad of pink tissue stretched across the top of the choanae. The larynx was red and œdematous and the swelling of the false cords partly hid the true cords which were thickened, greyish and more or less fixed in an adducted position leaving a very narrow glottis. Bronchoscopy showed a diffuse redness, somewhat granular, extending over the greater part of the trachea and right main bronchus. A biopsy taken from the right side of the nasal septum showed granulations typical of rhinoscleroma with a diffuse infiltration by inflammatory cells, plasma cells predominating. There were also Mikulicz cells containing short thick Gram-negative bacilli, and hyaline eosinophil nucleated masses of Russell bodies (Figs. 1 and 2). A blood count showed a relative mononucleosis of 12 per cent.

He was given a course of deep X-ray therapy in December, 1947, and January, 1948, to the respiratory tract without any appreciable effect and in March, 1948, it was considered that there had been no significant change in the lesions and accordingly he was transferred to the Middlesex Hospital for treatment with streptomycin, which was not available at Mount Vernon Hospital at that time. Tomographs taken soon after his transfer showed considerable

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stenosis of the larynx with obliteration of the normal anatomy. The ventricles had been completely filled in (Fig. 3).

On April 14th he was started on streptomycin at a dosage of 3 gm. per day (0·5 gm. four-hourly). One month later there was definite improvement in the condition of the nose, but on May 12th the dosage of streptomycin had to be reduced to 2 gm. per day (0·5 gm. six-hourly) on account of toxic symptoms in the form of giddiness, nausea and anorexia. At that time he had received 84 gm. of streptomycin and the toxic symptoms disappeared within a week of reducing the dose. By the beginning of June his airway had improved so much that he was able to have his tracheostomy tube spigoted for up to two hours at a time and when the streptomycin was stopped on June 26th he was keeping the tube permanently closed. The total dose of streptomycin given was 173·5 gm. in 74 days.

When he was transferred back to Mount Vernon Hospital on July 15th there had been still further improvement. His voice was stronger and the glottis was much wider. There was some thickening of the false cords, but the true cords could now be seen easily and moved well. There was still crusting in the nose and nasopharynx. The tracheostomy tube was removed and the fistula allowed to contract.

In May, 1949, the patient was admitted to the Manchester Royal Infirmary and the tracheostomy fistula closed. A bronchoscopy at that time still showed some general thickening of the mucosa in the trachea and right main bronchus. When he was seen at Manchester in November, 1949, he was still a little hoarse but had a good airway and there was no crusting in the larynx although there was still some crusting in the nose.

Case II. K.L. Male, Age 25.

This man was born in Poland and lived there until 1940 when he was " transferred " to Russia which he " left " in 1941. Since then he has been in the U.K.

In April, 1944, he noticed some hoarseness and breathlessness which gradually increased and in August, 1944, he was admitted to the Paderewski Hospital, Edinburgh. He was found to have small nodules in the nose covered by purulent secretion and there was an area behind the right posterior faucial pillar which was similarly affected. In the larynx the airway was much reduced as a result of involvement of the inter-arytenoid region and bronchoscopy showed similar changes in the subglottic region and carina. The bronchi were not involved. A biopsy which was taken showed scleroma. He received a course of deep X-ray with improvement in the pharynx and larynx but not much change in the nose.

In April, 1946, he had to have an emergency tracheostomy but this was soon allowed to close and did not have to be reopened at any later stage.

He was admitted to Mount Vernon Hospital in June, 1948, in moderate general condition and with a healed tracheostomy scar. The inferior turbinates were inflamed and covered with crusts which bled when touched and there was an adhesion between the septum and the right inferior turbinate. There was a good deal of mucopus in the nose and nasopharynx. In the larynx the arytenoids were red and swollen and the glottis narrow, but both cords moved,

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although there was less movement of the left than the right. He received a further course of deep X-ray to the larynx and trachea and direct radium application to the nasopharynx with definite improvement in his general condition and in the local lesions. In spite of this it was considered that he should be given a course of streptomycin in view of the improvement which it had produced in the previous case.

Accordingly in October, 1948, he was transferred to the Middlesex Hospital. At that time he still had some crusting in the nose and there was patchy white membrane in the nasopharynx. The vocal cords were mobile but there was œdema of the aryepiglottic folds and membrane in the subglottic region. Bronchoscopy revealed crusting in the posterior commissure and in the upper two-thirds of the trachea. A piece of tissue, which was taken from the anterior wall of the trachea, and sent for culture grew the following organisms :

(1) Moderate K. pneumoniae—sensitive to streptomycin.

(2) Profuse C. diphtheriae gravis—sensitive to penicillin and streptomycin (subsequently shown to be avirulent).

(3) Moderate β-hæmolytic streptococci—sensitive to penicillin.

A culture which was set up for M. tuberculosis gave no growth after three months.

The K. pneumoniae was found to give the following fermentation reactions :

Lactose	Dextrose	Maltose	Mannite	Sucrose	Indole	Nitrate reduction
—	Acid	Acid	Acid	—	—	+

In view of the bacteriological report the patient was first given a course of 4,000,000 units of penicillin in 5 days. A nasal swab then grew commensals only and a throat swab grew moderate β-hæmolytic streptococci and no KLB. Accordingly he was started on streptomycin at a dosage of 2 gm. per day (0·5 gm. six-hourly). A throat swab taken a fortnight later grew no pathogenic organisms.

On December 10th, after 44 gm. streptomycin had been given in 22 days, the dose had to be reduced to 1 gm. per day (0·5 gm. b.d.) on account of commencing giddiness with nystagmus. A week later the streptomycin was stopped at a total dose of 50·5 gm. in 30 days. There was still some submucous infiltration of the arytenoid region but the throat looked better on the whole. Benadryl which he was given for the toxic effects of streptomycin had no apparent effect. An audiogram showed only slight loss in some frequencies and caloric tests showed no response to water at 30° C. or 44° C. for 40 seconds, or to water at 23° C. for 1 minute.

At the end of January he was discharged from hospital much improved and when he was seen at the end of March he had no pain and his voice was improved. There was minimal crusting in the upper respiratory tract. When he was re-examined in May, 1950, his only symptom was huskiness. There was some generalized redness of the interior of the larynx but no infiltration, fixation or crusting. The nasal mucosa was normal but there was some very slight atrophy in the nasopharynx, possibly due to the radiation. He was apparently completely cured of scleroma.

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The tomograph was taken by the X-ray department of the Middlesex Hospital.

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