Letter to the Editor

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Statement Regarding the Resurgence of Tuberculosis

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Introduction

Tuberculosis is as old as mankind. Prehistoric skeleton remainders and mummies show abnormalities the tuberculous nature of which has been proven. Tuberculosis is the best documented cause of death of all times. In the past 200 years more than 1 billion people died of this disease. In Europe around 1900 1 of 5 patients died of tuberculosis. It was considered a major threat to western civilisation. Following the introduction of streptomycin, the first antibiotic for tuberculosis in the late 1940s, later by isoniazid, rifampicin, etham-butol and, more recently, pyrazinamide and amikacin and the annual natural decline of tuberculosis of 5%, it looked as if tuberculosis was about to be eradicated in the western world. However, since the mid 80s the initial optimism has been replaced by serious concern about the world-wide resurgence of tuberculosis.

The rising incidence in developing countries was outlined by Stanford et al. [1] in their paper with the provocative title 'Is Africa lost?'. They suggested that the world was facing the greatest public health disaster since the plague. The World Health Organisation (WHO) [2] declared tuberculosis the 'global emergency' in 1993. The recent estimated increase in notification rates of tuberculosis in Europe varies between 1.6% (Sweden) and 33.3% (Switzerland) per 100,000 yearly.

The WHO estimates that in this decennium yearly 10 million new cases of active tuberculosis will occur of which 35% will die. This means that in this decade 30 million people will die of tuberculosis and that around the year 2000 two milliards will be infected¹, accounting for 1/3 of the world population [3].

The majority of cases of tuberculosis occur in the developing countries. The deceased represent 25% of the avoidable deaths in these countries. Moreover 75% of the tuberculosis patients are between 15 and 50 years of age, the economically active part of the population. At present the most dramatic increase of tuberculosis appears to occur in South Africa, with a rate of 311 per 100,000/year. In developed countries the increase of incidence of tuberculosis is

¹ The term infection has been used to indicate that live tubercle bacilli exist in the body and have the potential to become reactivated. The tuberculosis disease state is synonymous with disease activity and symptoms. In infected persons with normal immune reactivity active tuberculosis may occur during life in 5% of cases, whereas the presence of AIDS or serological positivity to HIV increases the risk 170-fold and 130-fold, respectively.

mainly caused by (1) a decrease of immunisation programmes; (2) discontinuation of periodic population examination; (3) an increase of emigration from countries with a high incidence of tuberculosis, and (4) the development of drug multi-resistance to mycobacterial strains.

In developing countries the increase in incidence of tuberculosis is related to the infra-structural problems with the result that less people receive treatment. Untreated, 50% of patients die within 2 years during which period each case has caused 10-20 new cases. Nowadays in developing countries the rising incidence of tuberculosis is particularly related to the increase of patients with HIV infection. In Africa one quarter of tuberculosis cases is HIV-attributable [4].

Mycobacterial Infections, HIV and AIDS

World-wide, pulmonary tuberculosis is the most common concomitant HIV-related opportunistic infection. Particularly in Africa, India and Brazil tuberculosis goes hand in hand with the distribution of HIV infection. There are apparent clinical differences in pulmonary tuberculosis cases between non-HIV-infected and HIV-infected patients: in the latter upper lobe cavity disease is more exceptional and diffuse interstitial abnormalities more usual. It makes the diagnosis more complicated. The incidence of extra-pulmonary tuberculosis increases as well, in particular in immune-compromised patients where it exceeds pulmonary tuberculosis 2-3 times. In HIV-infected patients with tuberculosis, the tuberculous involvement is in 35-40% pulmonary, in 25-35% extra-pulmonary and in 35-40% both pulmonary and extra-pulmonary.

Not only infections due to *Mycobacteria tuberculosis* have increased in the past decade, also infection due to non-tuberculous mycobacterial (NTM) (synonyme atypical, and *Mycobacteria* other than tuberculosis), for both pulmonary and extra-pulmonary disease. Pulmonary disease is the most common form of NTM infections. It mainly affects individuals with AIDS. The most common strains are *Mycobacterium kansasii*, *Mycobacterium avium intracellulare* and *Mycobacterium scrofulaceum*.

In the United States and Africa the incidence of extra-pulmonary tuberculosis increases 2- to 3-fold the incidence of pulmonary tuberculosis.

Mycobacterial Infections in the Head and Neck Region

It is to be expected that in the head and neck region mycobacterial and NTM extra-pulmonary manifestations will increase in number.

ENT surgeons should be aware of this growing problem and rank

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tuberculosis higher in the list of differential diagnoses of the disorder encountered.

Extra-pulmonary tuberculosis of the mucus of the head and neck region mainly occurs by bronchogenic route, secondary to pulmonary tuberculosis, but spread by the haematolymphogenic route is also possible. NTM infections arise mainly as a primary infection. Atypical *Mycobacteria* are ubiquitous. They are found in soil, water, plants and animal excretions. The different strains have a low pathogenicity in the normal host. There is no evidence of direct person-to-person transmission. The organisms are often resistant to the usual anti-tuberculous agents. It has to be realised that the clinical presentation of extra-pulmonary tuberculous manifestations may differ from the classical description in particular in patients with HIV infection or AIDS [5, 6].

The clinical presentation of mucosal lesions is usually not specific: the granulomatous or ulcerative lesions may mimic malignancy and even combinations of pulmonary tuberculosis, laryngeal tuberculosis and laryngeal cancer have been described. Tuberculous cervical lymphadenitis develops in approximately 5% of all patients with tuberculosis. The nodes usually present in the posterior triangle and in most cases are matted together. Definitive diagnosis is made by means of tissue biopsy or fine needle aspiration (neck glands) and mycobacterial tissue culture. Recent molecular biological techniques as the polymerisation chain reaction are valuable new diagnostic tools.

Before the introduction of anti-mycobacterial drug treatment, tuberculous laryngitis was the most common chronic laryngeal disorder in Europe and North America with the prevalence of approximately 30% among patients suffering from pulmonary tuberculosis. Autopsies of these patients reveal that this complication is overlooked in as many as one third of the clinical diagnoses.

In the developing world tuberculous laryngitis is probably still a common complication [7]. It is remarkable that in publications dealing with autopsies of patients who died of AIDS and tuberculosis up till now manifestations in the ENT area have not (yet) been included [6, 8]. Tuberculous lymphadenitis is the most common manifestation of mycobacterial or NTM infection in the neck. The latter is much more common.

The treatment consists of standard anti-mycobacterial medication. The anti-mycobacterial medication presently recommended

consists of an 'intensive phase' of 2 months with daily intake of iso-niazid, rifampicin and pyrazinamide, and a 'continuation phase' of 4 months with daily intake of isoniazid, rifampicin and ethambutol. For patients who have been treated before or are HIV-positive the recommended treatment consists of 2 months' isoniazid, rifampicin, pyrazinamide, ethambutol (or amikacin) followed by 4 months pyrazinamide, rifampicin, ethambutol (or pyrazinamide) till the resistance pattern is known. Outpatient treatment is generally preferred.

The NTM infection is quite resistant to the present anti-mycobacterial drugs, though combination with claritromycin seems promising [9]. Surgery may be necessary particularly in case of persistent lymphadenitis. In summary, the recent resurgence of tuberculosis requires a great awareness of the otorhinolaryngologist and head and neck surgeon of an extra-pulmonary tuberculous manifestation of the disease encountered.

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