Infectivity of patients with pulmonary tuberculosis during chemotherapy

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In the current number of the Journal, Clancy et al. [1] have examined 29 specimens of sputum from patients before and during chemotherapy by direct smear, culture, and guinea-pig inoculation with the aim of deciding whether there is any change in pathogenicity during the early weeks of chemotherapy. They found that the occurrence of tuberculosis in the guinea-pig was more closely associated with the results of culture than with the duration of the therapy received by the patient at the time of collection of the specimen and conclude that a change in pathogenicity of the tubercle bacilli as a result of treatment was unlikely to have occurred. They raise the question of whether patients with "sputum positive tuberculosis", despite being on effective chemotherapy, can be regarded as non-infectious, especially as they may be in contact with other immunocompromised patients. Now, "sputum positive" implies a smear-positive or a culture-positive result. There is, however, a high incidence (20-60%) of smear-positive, culture-negative specimens in the first few months of short course therapy [2], perhaps due to retention of acid-fastness by bacilli killed by the antituberculosis drugs. Thus, it would be more appropriate to consider only the infectiousness of culture-positive tuberculosis. The distinction is important, particularly in developing countries, where routine cultures for tubercle bacilli are rarely available. Controlled studies show that sputum culture conversion is very rapid; 85-90% of initially smear-positive patients treated with currently recommended short-course regimens containing rifampicin and pyrazinamide have negative cultures at 2 months and only an occasional scanty positive culture is obtained from any of them thereafter [3-6].

What then are the risks of infecting contacts during the initial period of treatment while cultures and guinea-pig inoculation may still be positive? Untreated patients seldom have counts of over $10^7$ colony forming units of Mycobacterium tuberculosis per ml sputum, while $10^3$ is a more usual count for smear-positive patients. At 8 weeks, conversion has generally occurred so that these counts must then have fallen by about $10^{4-10}$. Data from Jindani et al. [7] suggests that sputum counts from patients on regimens containing isoniazid, rifampicin and pyrazinamide fall by about 20-fold in the first 2 days and by a further 200-fold in the next 12 days to reduce the counts of an initially smear-positive patient to about $10^6$ per ml at 2 weeks, a level below the estimates of $10^{4-10}$

per ml which are the limits indicating a change from smear-positive to smear-negative, culture-positive in untreated patients [8]. Contact studies have shown that smear-negative patients are not infectious [8, 9]. Furthermore, there are several reasons why a patient under treatment is less infectious than an undiagnosed case in a contact study. The period during which infection can be transmitted is much shorter, a matter of days rather than months or even years. The volume of sputum and the amount of coughing are both rapidly reduced by treatment. Instruction should be given to make coughing less dangerous [10]. The Madras home/hospital study has shown that contacts of patients with pulmonary tuberculosis were infected before diagnosis of the index case and that the incidence of tuberculosis among them was not influenced by segregation of the patients in sanatorium [11, 12]. Even though the Madras study might not have been able to detect a very small risk of infection from a patient because of the high prevalence of tuberculosis in the environment, we can conclude from all of these considerations that the risk of transmitting infection, particularly after the first two weeks of treatment, is negligible.

Does the presence of immunocompromised patients in the ward alter this conclusion? An infection with tubercle bacilli is almost always caused by droplet nuclei which are small enough to reach the terminal alveoli of the lungs, and does not result from contact with larger droplets or from fomites. This is why tuberculosis is less infectious than might be expected from the number of viable bacilli in sputum. From the work of Rius [13], it seems that an infection, signalled by tuberculin conversion, can result in man as in the guinea-pig from a very small number of bacilli, probably 3 or less, reaching the alveoli. The chance of such an infection occurring would be the same in an immunocompromised patient as in one with normal immunity, though the consequences of the infection would be different; the likelihood of progression of the infection and its speed would be greater. In the Madras study, tuberculin conversion occurred at equal frequency in contacts of home and sanatorium patients [11], and indeed the failure of smear-negative patients to cause disease in other contact studies [8, 9] must reflect a similar failure to infect them. We can conclude that there is little reason to segregate tuberculous and immunocompromised patients, apart perhaps for the first two weeks of treatment when there might still be a remote chance of transmitting infection.
References

5. East African/British Medical Research Councils. - Controlled clinical trial of 4 short-course regimens of chemotherapy (three 6-month and one 8-month) for pulmonary tuberculosis. *Tubercle*, 1983, 64, 153-166.