

268. Substandard tuberculosis drugs on the global market and their simple detection.

Laserson KF, Kenyon AS, Kenyon TA, Layloff T and Binkin NJ, Department of TB Elimination, Centres for Disease Control & Prevention, Atlanta, Georgia, USA : **Int J TB & Lung Dis** **2001, 5, 448-454.**

Sub standard drug preparations are present throughout the world. Poor quality of drugs could be due to various reasons varying from manufacturing practices to storage. Substandard drugs can have devastating clinical and economic effects, leading to drug resistance, prolonged illness, and adverse reactions, including death. The global prevalence of substandard anti tuberculosis drugs has not been systematically assessed. Lack of facilities in the high burden countries is an important reason for not making such assessments. To maximize the effectiveness of tuberculosis control efforts, simple, inexpensive drug quality screening methods are needed. The Thin Layer Chromatography (TLC) method is an accepted and WHO recommended method for making such assessments. It is 98% sensitive and specific and was used in this study.

Isoniazid (INH) and Rifampicin (RMP) single and fixed dose combination (FDC) formulations were collected from selected TB^C Programs and pharmacies in Colombia, Estonia, India, Latvia, Russia and Vietnam. Samples were screened using a recently developed TLC kit. All abnormal samples and 40% random sample of normal formulations were further analyzed using confirmatory techniques. Samples outside of 85% to 115% of stated content, and/or containing compounds other than the stated drug, were defined as being substandard.

Overall, 10% of all samples, including 13% RMP samples, contained <85% of stated content. More FDC (21%) than single drug samples (13%) were substandard. A comparison of TLC with the confirmatory analysis for RMP analysis showed a sensitivity of 100%, a specificity of 92 %, a positive predictive value of 67%, and a negative predictive value of 100%. An analysis of INH showed a specificity of 90%. The other three parameters for INH could not be determined. A substantial number of anti tuberculosis drugs from several countries, in particular FDCs, were found to be substandard. Such drugs may contribute to the creation of drug

resistant tuberculosis. TLC is an effective, convenient and inexpensive method for the detection of substandard drugs.

269. Transmission of Mycobacterium tuberculosis depending on the Age and Sex of source cases. Borgdorff MW, Nagelkerke NJD, W de Hass PE and Soolingen Dick, Royal Netherlands TB Association, Hagere; Netherlands : **Ame J of Epidemiology**; **2001, 154/10, 934 -943.**

Tuberculosis is an important cause of global mortality and morbidity especially in the developing countries. In the low prevalence countries (eg. Western Europe) tuberculosis is changing from an endemic disease to a disease associated with immigration and risk groups. In these countries emphasis is given to active case finding. The aim of active case finding is to detect tuberculosis cases early in the course of the disease to prevent development of severe disease and to limit transmission by reducing the infectious period. To focus active case finding on the most infectious cases, it would be useful to know which types of source cases are particularly effective in generating secondary cases. Recently DNA finger printing has been used in population based studies to determine the average number of infectious tuberculosis cases generated by a source case. The objective of the present study was to determine to what extent transmission of Mycobacterium tuberculosis from tuberculosis source cases is associated with the age and sex of the source case. The study used DNA finger printing in a population based study in the Netherlands during the period 1993 -1998.

DNA finger prints of Mycobacterium tuberculosis isolates were matched to patient information in the Netherlands Tuberculosis Register for 1993 -1998. Clusters were defined as groups of patients with pulmonary tuberculosis whose isolates had identical DNA fingerprints. Source cases were assigned by using two models. The first case model assumed that the first diagnose case was the source case. The incidence rate model estimated source case probabilities from the incidence rates of potential source cases and the time of diagnosis.

DNA finger prints of 6,102 isolates were matched to patient information on 5,080 (83%) cases, of whom, 3,479 had pulmonary disease. According to

both models, the number of infectious cases generated per source case was lower for female than for male source cases and decreased with increasing age of the source case. The authors concluded that transmission of tuberculosis is associated with the age and sex of source cases as well as the age of secondary cases. Increased transmission among immigrant groups in the Netherlands is largely attributable to the relatively young age of immigrant source cases.

270. DOT for patients with limited access to health care facilities in a hill district of Eastern Nepal. Wares DF, Akhtar M & Singh S, TB & Rehabilitation Training Centre, Addis Ababa, Ethiopia : **Int J TB & Lung Dis, 2001, 5, 732-740.**

Tuberculosis is an important health problem in Nepal, with an estimated 60% of the adult population being infected with Tuberculosis. Despite the implementation of a much improved National Tuberculosis Programme (NTP), 8000-11,000 people still die from TB each year in Nepal. The Directly Observed Treatment Short course (DOTS) strategy is being promoted by international agencies for improving treatment outcomes for tuberculosis. The objective of this study was to compare results before and after a decentralised DOT intervention

Patients registered in Dhankuta district, Nepal, from 1996 - 1999 were enrolled in the study. The 1,79,131 population of this district is scattered over a wide area of 891 km² in a difficult terrain. Health care facilities are not easily accessible because of the hilly terrain. Patients received their intensive phase treatment under health workers supervision via one of three DOT options : 1) Ambulatory from the peripheral government health facilities; 2) Ambulatory from an international non-governmental organisation (INGO) TB clinic in district centre; or 3) Resident in INGO TB hostel in district centre. Historical data from 1995-1996, with unsupervised short course chemotherapy, were used for comparison.

For the 307 new cases, smear conversion at two months was 81.6% vs. 58.8% for historical, $P=0.0001$. Cure rates were 84.9% for new cases vs. 76.7% for historical, $P=0.03$. Overall costs to the INGO provider fell by 7%, mainly as a result of staffing reduction in the INGO services made possible by rationalisation with government services during the intervention.

By offering varied DOT delivery routes including an in-patient option, satisfactory results were possible with DOT even in areas where access to health care facilities was difficult. Provision of in-patient care via an INGO TB hostel allowed a significant proportion of new cases 31% to receive their intensive phase treatment who otherwise may have had difficulty accessing treatment, due either to the distance to the nearest health facility or to disease severity. Substitution of government hospital beds or local hotel beds for the INGO hostel beds may allow the model to be reproduced elsewhere in similar geographical conditions in Nepal, but further studies should be performed in a non-INGO supported district beforehand.

271. Evidence for action? Patterns of clinical and public health research on tuberculosis in South Africa, 1994-1998.

Pillay V, Swingle G, Matchaba & Volmink J, South African Cochrane Centre, Medical Research Centre, Tygerberg, South Africa : **Int J TB and Lung Dis, 2001, 5, 946-951.**

The most commonly notified disease in South Africa is Tuberculosis (TB). Progress in the control of the disease has been slow with the incidence of the disease gradually increasing since 1993. The clinical and public health research done in this field should be meaningful to potential users of the information. The objective of this article is to describe patterns of clinical and public health research into TB in South Africa from 1994-1998, and to assess the quality of studies of diagnostic accuracy and treatment.

MEDLINE and the African Health Anthology were searched for journal articles published from 1994- 1998 reporting clinical and public health research into TB in South Africa. Information extracted from the reports included research setting, study design, aspects of the quality of study design and reporting, and evidence of attention to statistical power. Three reviewers independently assessed the first fifty randomly- sampled articles, in order to develop and improve the data extraction form, develop a uniform interpretation of the information provided in the articles and evaluate and improve the data extraction skills of the first author.

One hundred and thirty five eligible studies were identified. Case reports or case series formed 39 (28.9%) of the studies. Important methodological flaws were identified in studies of diagnosis and treatment that compromised the validity of the study

results. Of the 28 studies assessing interventions, 10 (35.7%) were randomized controlled trials with only one reporting adequate allocation. Of the 34 studies assessing diagnosis, 16 (47.0%) were cross-sectional assessments of diagnostic accuracy, and none reported that comparison of the reference standard was independent or blind. Fifty four (79.4%) of the analytical studies with statistically non-significant results showed no evidence of consideration of sample size. Hence the usefulness of TB research in South Africa is compromised by the questionable validity of many studies and a lack of attention to sample size.

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272. Exogenous Reinfection with Tuberculosis on a European Island with a Moderate Incidence of Disease.

Caminero JA, Maria J. Pena, Maria I. Compos-Herrero et al. Service of Pneumology, University General Hospital, Spain : **Am J Respir Urit Care Med** 2001, **163**, 717-720.

The incidence or the frequency of reinfection by *M. tuberculosis* in treated patients may be due to a number of factors which include genetic mechanism of the individual (immune suppression as in the case of HIV patients) or due to the high virulence of *M. tuberculosis*. Initially, it was thought that the high rate of tuberculosis in the community was the cause of high rate of reinfection (endogenous reactivation). However, with the use of genotyping techniques, it was demonstrated that exogenous re-infection not only occurs in immunocompromised HIV patients but is also in non HIV patients.

In a study conducted by Camminero JA et al in Gran Canaria Island, Spain between 1991 and 1996, 962 cases with culture positive tuberculosis were selected for IS6110 based RFLP analysis. Twenty three patients with culture positive on two occasions (12 months apart) were selected. Of these, 5 were excluded because of non availability of bacterial DNA for genotyping analysis. The Results revealed that 8 patients had exogenous reinfection, of which, 6 were HIV seronegative and 2 were HIV seropositive. The remaining 10 patients showed endogenous reactivation. Three of these developed MDR tuberculosis

This population based study provides insight into the manner in which reinfection (exogenous

reinfection and endogenous reactivation) occurs. While in case of reinfection in defaulters, it is by the same organism that caused the initial infection, reinfection in cured patients is by a totally new organism. This is mostly due to the immune suppression as in case of HIV patients. Hence, tuberculosis control programmes and the people associated with it must pay more emphasis on completing the therapy of the initial episode of tuberculosis, thereby minimizing endogenous reactivation, MDR Tuberculosis in case of defaulters and also preventing reinfection in previously cured patients.

273. Tuberculoma in pregnancy

Pandole A, Akolekar R & Vaidy N, et al.: Dept of OBG and Gynaec, LTMG Hospital, Sion, Mumbai ; **Bombay Hospital Journal** 2001, **43**,200-201.

Tuberculosis being common disease in developing countries as ours makes tuberculoma quite a likely diagnosis in many patients with symptoms of raised intracranial pressure. The situation becomes even more complex when patient with tuberculoma is pregnant. It therefore quite likely that a pregnant patient with history of convulsions may have tuberculoma.

A 19-year-old patient (pregnant) was referred to Dr. Pandole A et al., with history of two episodes of convulsions with 8 months of amenorrhea. She had no history of any trauma or head injury in the recent past. She had no headache preceding the convulsions, no major obstetric complaints and could perceive good foetal movements. She was drowsy. A CT scan revealed lesions in parietal and temporal lobe suggestive of tuberculoma. A chest radiograph was suggestive of pulmonary Koch's. The baby was delivered by Caesarian section and after 5 days, excision of tuberculoma was done, Histopathology of this intracranial mass confirmed tuberculoma and the patient was put on Anti-tuberculosis drugs.

The diagnosis of tuberculoma is difficult during pregnancy because of its similarity with eclampsia. If on a CT scan an isodense ring with perilesional edema that persists for few weeks is detected, it is suggestive of tuberculoma. Hence, CSF examination, CT scan with proper clinical correlation should be emphasized.

274. Tuberculosis Prevalence in an urban jail White MC, Tulskey JP & Portillo CJ et al : Department of Community Health Systems,

University of California, School of Nursing, San Francisco, USA : **Int J TB & Lung Dis** 2001, 5 (5), 400-404.

By the year 1998, there was a considerable decline in the report of active tuberculosis cases in USA. However, among the jail inmates, there was a steady increase in the rate of active and latent TB infection (LIB). A study was conducted to document the change in TB prevalence in the San Francisco city and county jail.

The period prevalence analyses were done for 1994 and 1998. The sample included all person booked into jail during the two years. Prevalence of active TB was 72.1/100000 jail population for 1998 and did not change significantly from 1994. The prevalence of active TB among Latinos was higher than that of the black or white inmates and 24% higher in 1998 than it was in 1994. Latinos in this study represented 20.1% and 17.7% of inmates booked into the jail in 1994 and 1998, but accounted for 43.0% and 41.7% of the LTB found at completion of screening in the two years.

Reasons for high prevalence of TB infection within jails is the disproportionate number of inmates, members of ethnic and racial minorities, substance abusers and HIV persons. Screening for TB among jail inmates is an increasingly valuable clinical and epidemiological tool for case finding and identifying persons who would benefit from preventive therapy.

275. A comparison of unsupervised treatment along with intensive health education and Directly Observed Treatment in Pulmonary Tuberculosis.

Prasad .R, Rixavi DM & Kant S et al., Dept. of TB and Chest diseases, King George's Medical College, Lucknow: **Ind J Tub** 2001,48,21-24.

Directly observed Treatment (DOT) as a means of Anti-Tuberculosis Therapy/Treatment (ATT) was devised to improve the patients' adherence to ATT. The authors are of the opinion that despite of being very effective, it also has some drawbacks such as high cost and in many situations it may be inefficient, impracticable to give DOT for all patients. Thus, a need was felt to experiment with alternative and less intrusive method of increasing patients' adherence to treatment.

This resulted in a study, which was conducted to evaluate the effect of intensive health education on treatment compliance and overall outcome as compared to that obtained from DOT. Out of total 89 patients studied, 51 patients were given drugs under direct observation (RNTCP Cat I) and 38 were given the same regimen unsupervised along with intensive health education. The treatment was successful in 46 (90.2%) of the patients on DOT and 34 (89.47%) of the patients on unsupervised treatment. 3 patients on both the groups defaulted.

According to the authors, the study thus indicates that by intensive health education to patients, the results obtained would be as good as those obtained by DOT. They conclude that, unsupervised treatment along with intensive health education can be practiced especially when DOT is either impracticable or is refused by patients.

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