Abstract
A six month study on three different anti-tubercular regimens was carried out in 160 patients between 19-60 years of age in the Gulab Devi Chest Hospital, Lahore from Junç 1980 to October 1981. This hospital has existed since 1934 and caters to patients suffering from chest diseases, mostly pulmonary tuberculosis. The patients selected for the trial had a positive sputum smear, clinical and radiological evidence of pulmonary tuberculosis and no other concomitant disease. Patients were hospitalized for the first three months and then treated on an outpatient basis for the following three months. Streptomycin, isoniazid, pyrazinamide and rifampicin were given in three different combinations. All patients showed a marked improvement clinically, radiologically, in weight gain and sputum conversion except six who had to stop the therapy due to side effects. 134 patients completed the trial with a few of them having untoward effects of a mild nature, such as joint pains, peripheral neuritis and a slight impairment of the liver function tests. The six months short course chemotherapy proved highly effective and advantageous (JPMA33 :243, 1983).

Introduction
The management of pulmonary tuberculosis has been completely revolutionised during the last four decades. The treatment began at the turn of the century, with plenty of fresh air, sunshine, a high protein diet, codliver oil and calcium. This was followed by the era of artificial pneumothorax, pneumoperitoneum, phrenic crush and thoracoplasty. Then came the drug regimen with streptomycin, PAS and INH with added resectional surgery. In 1960 PAS was replaced by ethambutol. Pyrazinamide, cycloserine, ethionamide, kanamycin, capreomycin and viomycin were added to the standard regimen with the passage of time. The duration of the anti-tubercular therapy always extended from 18-24 months and it is not surprising that many patients absconded from treatment before the end of the therapy. Consequently, from about 1970, workers have concentrated on reducing the time of treatment to more reasonable durations. These advances have become possible through the use of combinations of potent bactericidal agents which are capable of acting on the different populations of mycobacteria present in the human lesions (Mitchison, 1980). The bacilli, which are rapidly growing and extracellular, are destroyed by isoniazid, rifampicin and streptomycin. Those bacteria inside the macrophage or the walls of the tuberculous cavities are only affected by agents which penetrate the cell walls. These include isoniazid, rifampicin, and also pyrazinamide which is particularly bactericidal in the acid conditions found inside the cells. A third group are the near-dormant bacilli or persisters that metabolise infrequently and for which rifampicin has the most rapid bactericidal activity. This activity of rifampicin is particularly important since it sterilizes the lesions and reduces the possibility of relapse (Fox and Mitchison, 1975; Dickinson and Mitchison, 1976, 1981).

Intermittent drug administration with the required dose given twice a week has given encouraging results and relapse rates have proved to be low (Zierski, 1981).

Material and Methods
One hundred and Sixty patients of both sexes were selected for the trial. The criteria fulfilled were a positive smear of the sputum for AFB, an X-ray and clinical evidence of pulmonary tuberculosis and no serious concomitant disease as diabetes mellitus, malignancy. The ages of the patients ranged between 18 and 60 years, and only those cases were included who resided within ‘a twenty miles radius of the hospital.

The patients were hospitalized for the initial three months followed by three months treatment in the outpatients department. Sixteen patients had a minimal lesion with the others having advanced lesions with cavitation of various sizes.

The anti-tubercular drugs selected were divided into three groups in three different combinations (Table I).
23 patients followed the regimen of Group I, 41 of Group II and 70 of Group III. The dosage of the drugs given are shown in Table. II.
Six patients had to be excluded from the trial in the initial phase as they developed untoward reactions. One person died due to severe haemoptysis. Nineteen individuals left the trial for personal reasons and 134 patients completed the six months therapy.

Results

All 134 patients expressed a subjective feeling of well-being within a week of starting chemotherapy. Sputum conversion was fully achieved in the patients following the Group III regimen (2HRZ/4H₂R₂) within four months whereas 9% of group I and 13% of Group II patients remained sputum positive after six months of therapy (Table III).
87% of the cases belonging to the Group III regimen showed a marked radiological improvement at the end of the trial. 83% of group II and 74% of Group I also projected a better X-ray picture (Table IV).

The patients in all three groups had a gain in body weight and showed a fall in the E.S.R. at the end of the six months (Table V).
The haemoglobin rose in 91%, 95% and 97% of the cases in the three groups respectively and 5% of the patients in Group I had a decrease in haemoglobin whereas the rest remained unchanged. Side effects were observed joint pains in 22% of the cases of Group I and 11% in Group III, both groups which had pyrazinamide in the regimen. Those patients who did not receive pyrazinamide (Group III) did not have joint pains. Peripheral neuritis developed in 2 patients of Group I cases on daily isoniazid for six months. Mild purpuric rashes were noticed in 3 patients in Group III. Platelet counts remained within normal limits throughout treatment in these patients. Slight alteration in LFT’s were observed in all the 3 groups respectively (Table VI).

### Table – VI

<table>
<thead>
<tr>
<th>Treatment / Regimen</th>
<th>Group I 6SHZ</th>
<th>Group II 2SHR/4H₂R₂</th>
<th>Group III 2HZR/4H₂R₂</th>
<th>Drop Outs*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>23</td>
<td>41</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Joint Pains</td>
<td>5 (22%)</td>
<td>0</td>
<td>8 (11%)</td>
<td>1 in Group III</td>
</tr>
<tr>
<td>Peripheral Neuritis</td>
<td>2 (9%)</td>
<td>0</td>
<td>0</td>
<td>1 in Group I</td>
</tr>
<tr>
<td>Rashes:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Purpuric</td>
<td>0</td>
<td>0</td>
<td>3 (4%)</td>
<td>1 in Group III</td>
</tr>
<tr>
<td>b) Exanthemeic</td>
<td>0</td>
<td>1 (2%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Serum Transaminase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased With:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Hyperbilirubinemia and Clinical Jaundice</td>
<td>0</td>
<td>0</td>
<td>5 (7%)</td>
<td>3 in Group III</td>
</tr>
<tr>
<td>b) Hyperbilirubinemia Without Jaundice (Treatment Continued)</td>
<td>7 (30%)</td>
<td>1 (2.5%)</td>
<td>8 (11%)</td>
<td></td>
</tr>
</tbody>
</table>

*No. of patients included in total in whom side effects necessitated withdrawal of regimen.
Discussion

The results with these three course anti-tuberculosis regimens were found to be similar to the studies carried out by the Hong Kong Chest Service (1981) and East African Study (1981). All the regimens were effective in producing clinical, bacteriological and radiological improvement.

The relapse rates in the present trial are yet to be assessed. The results of similar studies (Group III 2HRZ/4H2 R2) as reported by Zierski (1981) show a relapse rate of 0% in a follow up period of 18 months in 84 patients. The regimen used in Group I (6 SHZ) had an 8% relapse in an East African Study (1974) carried out on 153 patients.

The incidence of side effects especially hepatotoxicity is particularly high in Group I (6 SHZ) which could be attributed to the use of daily pyrazinamide for all the six months (United States Public Health Service Tuberculosis Therapy Trial, 1959).

The patients being treated with the Group III regimen (2HRZ/4H2 R2) in this trial apparently experienced a higher incidence of side effects than in other studies (Hong Kong Tuberculosis Treatment Services/British Medical Research Council, 1976) though less than Group I (6SHZ) patients.

Despite the side effects, the majority of patients in this trial continued therapy for complete six months period and achieved satisfactory clinical results. The regimens containing two month of rifampicin, isoniazid and either streptomycin or pyrazinamide, followed by rifampicin and isoniazid for four months on a twice weekly basis appear to have the most promising results.

Conclusion

The short course anti-tubercular therapy regimen has proved to be highly effective and economical. The patient compliance is higher and side effects are minimal thus making this mode of treatment more acceptable.

Acknowledgement

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References

5. Hong Kong Tuberculosis Treatment Services/ British Medical Research Council (1976) Adverse reactions to short-course regimens containing streptomycin, isoniazid, pyrazinamide and rifampicin in Hong Kong. Tubercie, 57:81.
7. United States Public Health Service Tuberculosis Therapy Trial (1959) Hepatic toxicity of