INTRODUCTION

Tuberculosis (abbreviated as TB) tubercle bacillus or tuberculosis is often deadly infectious disease caused by Mycobacterium Tuberculosis. It is usually attacks the lungs (as pulmonary TB) but can also attacks the Central Nervous System, Lymphatic System, The Circulatory System, the Genitourinary System, Gastrointestinal System, Bones, Joints, and Skin

“Tuberculosis is contagious disease like a common Cold; it spreads through air only people who are sick with TB in their lungs are infectious. When infectious people coughing, sneezing, talking, or spit, they propel TB germs, known as bacilli into air. A person needs only to inhale a small number of these to be infected.

Epidemiology

It is surprising that in this World is newly infected with TB bacilli every second. Overall one – Third of the World population is currently infected with TB bacillus. Approximately 5-10 % of World population currently infected with TB bacilli (bat who are not infected with HIV- become sick or infectious at some during there life.

Global Regional Incidence: The world health organization (WHO) estimates that the larger number of new TB cases in 2005 occurred in South_ East Asia Region which are accounted for 34% of incidence cases Globally. However the estimated incidence rate in Sub_ Saharan Africa in newly twice that South_ East Asia Region, at nearly 350 cases per 100, 00 populations. It is estimated that 1.6 million deaths resulted from TB in 2005.

Drug Treatment of Tuberculosis

The goal of treatment is to cure the infection with drugs that fight the TB bacteria. The treatment of active pulmonary TB will always involve a combination of many drugs (usually four drugs) it is continued, (Rifampin,Isoniazid, Pyrazinamide and Ethambutol) It is continued until lab tests show which Medicines are best. Treatment usually lasts for 6 months, but longer course may be needed.

Daily Observe Therapy

In DOT patient swallows the medicines under the watchful eye of the doctor, a health worker, community volunteer, mohalla molvi, pharmacist, or even any entrusted family member. 12 the TB patients is almost always cured if these medicines are taken regularly for the entire period of time. The anti-tuberculosis drugs in
this short-course chemotherapy are Isoniazid, Rifampicin Pyrazinamide and Ethambutol or streptomycin.

DOTS stop TB bacteria at the source. Curing a contagious patients is the best way to prevent TB bacteria from spreading to others.4

“A single case of tuberculosis can spread the disease to 10-15 persons on average.2. DOTS (Directly observed treatment, short course) were devised as a response to the public health challenge of non-adherence and maintaining long term treatment for tuberculosis. DOTS have the following essential components. (for the discussion of all the five components of DOTS and its implementation see WHO, 1999).

(a) A regular uninterrupted supply of all essential anti TB drugs backed by governments’ commitment to sustained TB control activities.

(b) Standardized treatment regimen of six to eight months chemotherapy under supervision. In many LAMICS the role of DOTS supervisor is assigned to a family or a community member who regularly administers the drugs under close monitoring by a health worker.

The World Bank considers DOTS to be one of the most cost effective health interventions. DOTS are more cost effective than self-administered treatment. “Isoniazid-It is still considered a primary agent for chemotherapy of tuberculosis. It was discovered in 19 45, by cohrin, reported that nicotinamide possess tuberculosis action. Ebonized is the hydrazide of iboricotoric acid,

“It inhibit mycolic acids, an important constitute mycobacterium cell wall. Its mechanism of action is complex, with resistance, mapping to mutations in five different genes (Kat G, inh A, aph c kas A and ndh). It is orally absorbed in 1 to 2 hours. 75% to 95% excreted urine in 24 hours. Acetylisoniazid and Isonictonic acid are metabolites for excretion .It is still most important drug
world wide for the treatment of all types of Tuberculosis. The dose of 5mg 1 kg with maximum 300 mg

“A case of severe febrile reaction to INH is described. The patient had a mid febrile reaction two weeks following INH prophylaxis. Isoniazid was discontinued an initial mild febrile reaction to INH is warring sign that rechallange can result in a life-threatening situation”.

Toxic effects are usually encountered only with higher doses of Isonaizid. The incidence of adverse affects at higher dose of 10 mg 1kg has been reported to approximately 15%. CNS peripheral neuropathy occurs mostly in malnourished and preceeded by parathesias of feet and hands, convulsions, toxic encephalopathy, optic neuritis and atrophy. GIT nausea, vomiting, epigastric distress. Hepatic: elevated serum amino transfers (ALT, AST) and bilirubin concentration (10 to 20%) sometime it will become fatal. Hematologic: Agranuloytosis, Hemolytic Anemia, Thrombocypenia, Esinophilia.

Hypersensitivy: Fever, Skin eruptions (morbilliform, macupapular, purpuric or exofoliutive), lymphadeno-pathy, vasculitis.

Metabolic and Exocrine: Pyridoxine defiency. Pellagra, Hyperglycemia, Metabolic acidosis, Gynecomastia. Over dosage: symptoms are manifested in 30 minutes to 3 hours nausea, vomiting, dizziness, slurring speech, blurring of vision and visual hallucination. CNS: coma, intractable seizures.

EXCLUSION CRITERIA
- Patients suffering from liver disease.
- Patients suffering from cardiac disease.
- Patients suffering from renal disease.
- Patients suffering from diabetes mellitus.
- Patients suffering from other respiratory disease.
- Patients suffering from HIV infections.
- Pregnant or nursing women.
- Patients with previous multiple drug resistance.

The study period extended up to 24 weeks and 12 follow up visits of patients were taken. The required information such as name, age, sex, occupation, address, details of follow up visits and laboratory investigations etc, of each patient were recorded on proforma especially designed for this study. The selected patients were divided according to untoward effects of drugs during study period.

Ethical Issues
Patients were enrolled into the study only after informed consent, which was obtained from both the parent and care giver (first degree relatives as for as possible). The patient and care givers were given the deals about the purpose of the study and possible side effects. Only those who gave there consent included and patients were allowed to with draw there consent any time during any stage of the study. They were assured withdrawal from the study would not affect their further treatment.

INCLUSION CRITERIA
The 120 newly diagnosed patients of pulmonary tuberculosis, enrolled is this study after taking informed and written consent.

The patients were selected as diagnosed cases of pulmonary tuberculosis from medical chest OPD and chest ward of Muhammad medical college Mirpurkhas. Out of these patients were associated through out the study period.
- Diagnosed cases of pulmonary tuberculosis.
- Sex either male or female.

Control Group:

MATERIAL AND METHODS
This study was carried out in the department of Pharmacology and Therapeutics, collaboration with Free T.B Clinic of Muhammad Medical College Mirpurkhas Sindh, Pakistan, under kind supervision of Dr, SHAMIM-UR-REHMAN, Head of Department from, June: 2007 to Dec 2007.

All patients, in this study, were selected according to following criteria:

Group A: In the group INH 60 patients were included who manifested the Hepatitis and Peripheral Neuropathy in different gender.
Group B: In the group Placebo 60 patients was included who did not manifest side effects of drug.

MATERIALS
Isoniazid – 5 mg/kg
Placebo tablets (multivitamins)
LFT KITS

RESULTS AND OBSERVATION
In Table (I) and Figure-1 and 2 Isoniazid manifested Hepatitis in n=10 (16.3%) and 50 (83.3%) were negative in the patients of P.T.B, and peripheral neuropathy manifested 11 (18.3%), and 49 (81.7%) were negative. In placebo group there was no adverse drug reaction were noted.

This Table showed highly significant statistically.

In Table No: II and figure 3, 4 Isoniazid and placebo manifested the untoward effects of peripheral neuropathy and hepatic according to gender of P.T.B patients. Isoniazid produced 6 (60%) in male and 4 (40%) in female patients out of total 10 adverse reactions of INH in placebo nil. In case of peripheral neurological INH produced 7 (63.6%) in male and 4 (36.3%) in female and placebo produced nil in both sex.
DISCUSSION

Our study match with R.B. Byrd, B.R Horn, in which one thousands patients receiving 150 Isoniazid chemo prophylaxis were prospectively followed up to assess the value of liver function monitory plus, monthly clinical evolution. Two hundreds patients elevated SGOT level during course of treatment. No patients become seriously ill, and there were no deaths. Biochemical monitoring should do routinely in patients receiving Isoniazid chemo prophylaxis to avid development of revisable hepatic reactions.

"Peripheral neuropathy is associated with the use of Isoniazid but is uncommon at doses of 5 mg /kg. Persons with condition in which neuropathy is common (e.g. diabetes uremia, alcoholism, malnutrition, HIV infection ) as well as pregnant women and person with seizures disorder may be given pyridoxine 10- 50 mg (day) with Isoniazid treatment for latent TB infection."

Isoniazid is increasingly being used to control the spread of tuberculosis. It causes recurrent seizures profound metabolic acidosis, coma and death, in adults, to toxicity can occur with acute infection of 1.5 gram of Isoniazid doses larger them 30 mg per kg often produce seizures. Isoniazid toxicity usually appear 30 minutes includes nausea, vomiting slurred speech, dizziness, tachycardia, urinary retention, followed by stupor coma, recurrent grand mal seizures and hepatitis.

**CONCLUSIONS**

It proved that like other anti-biotic streptomycin must be careful in therapy of Anti-Tuberculosis Therapy.

The major side effects are those giving rise to serious health hazards, and require discontinuation of the drug and referral to chest physician. Minor side effects cause relatively little discomfort; they often respond to symptomatic or simple treatment but occasionally persist for the duration of drug treatment. Chemotherapy should be stopped or temporarily interrupted only of severe drug reactions.
intolerance toxicity occurs. In fact tuberculosis drugs are relatively toxic and mild side effects are not uncommon but most do not warrant drug withdrawal.

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Never deprive someone of hope; it might be all they have.

H. Jackson Brown Jr.