

# SEASONAL VARIATION OF A GROUP OF TOXICITY TO THIOACETAZONE\*

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## Introduction

It has been established by now that combination of INH and thioacetazone is as effective as INH and PAS. The doses have also been standardized (INH 30 mgs, and thioacetazone 150 mgs, per day). As this combination is most economical, less bulky and most convenient for self administration, we get maximum co-operation from the patients and greater therapeutic response during the course of treatment (2, 3, 4, 5, 8 and 11). This combination however has one disadvantage, i.e. higher toxicity (6) though some reports claim low toxicity for this combination in comparison to INH+PAS (5). Toxicity is thus the only handicap in the use of this combination.

This study is planned to draw attention to the incidence of toxicity and its relationship with the seasons and point out some probable association, so that a detailed and thorough study can be carried out in centres with better facilities for research.

## Material and Methods

This study is based on all tuberculous patients treated with INH and thioacetazone in 1965-69 in the Mana Camp, situated at a distance of about seven miles from Raipur city (M.P.). All of them were above 12 years of age, both males and females; and included patients treated both in the hospital and at home. They were in various stages of the disease, from advanced to minimal lesions; and bacteriologically, some were sputum positive and some negative. Most of them were refugees from East Pakistan, some were local from the nearby villages. Almost all of them were from low income group with poor nutrition and were living in congested houses with considerable over-crowding.

Climatically, the year in Mana can broadly be divided into three seasons :

1. *Winter Season* : From the month of

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In this preliminary report, the author has adduced evidence to suggest some relationship between thioacetazone toxicity and seasonal variations. This apparent association however could be due to some other factor and this needs thorough investigations, before the association can be accepted. The paper has been whetted by the Editors.

November upto the first half of February.

2. *Summer Season* : From the second half of February upto the month of June or July, depending on the onset of monsoon.
3. *Rainy Season* : From June or July upto the end of the October.

Humidity starts diminishing from November and is at a minimum from February to June, till the onset of the monsoon. Temperature rises gradually from the last half of February and reaches its maximum in the month of June or July. When the rains start, there is a sharp fall of temperature and rise of humidity. This persists upto the month of October, when the humidity starts falling gradually and the temperature also starts going down during winter from November upto the first half of February. The temperature ranges from 85°F to 119°F. Exact range of humidity is not known but is guessed from the dryness of the atmosphere, absence of rains, sensible perspiration, dryness of the soil and lowering of the subsoil water level etc. Efforts were made to get exact data regarding temperature and humidity range, but were not successful.

## Findings

Toxic reactions to thioacetazone have been studied in all patients put on INH+thioacetazone treatment since May, 1965. Table 1 shows the number of patients under treatment and the number of patients with toxic manifestations in each particular month. It is obvious from the table that the percentage of patients showing toxic reactions to thioacetazone is proportionately higher during the period February to July in all years. There is almost complete absence of toxic reactions from August to January inspite of the number of persons under treatment remaining more or less the same.

In almost all the above cases the drugs were stopped for a few days and then restarted. There was no recurrence of reaction except in seven cases where the combination had to be withdrawn permanently. Percentage of cases of toxicity where thioacetazone had to be permanently withdrawn is 10.29%.

There was some reduction in the occurrence of toxicity in the year 1967-1968 (in 1969 the

TABLE I

*Toxicity to Thioacetazone in proportion to the number of persons getting INH Thioacetazone combination per month*

Month	19 55	19 56	19 57	19 68	19 69
	Non Toxic	Toxic	Non Toxic	Toxic	Non Toxic
January	Nil	Nil	28	1	96
February	Nil	Nil	28	3	103
March	Nil	Nil	35	4	114
April	Nil	Nil	48	4	121
May	7	1	52	3	98
June	8		66	6	95
July	5	3	69	6	101
August	9	Nil	105	Nil	96
September	<sup>9</sup>	Nil	98	Nil	99
October	8	Nil	92	1	109
November	8	Nil	104	Nil	106
December	23	1	92	1	102
TOTAL	77	11	817	29	1240

\* Absence of toxicity which is found in the period of maximum toxicity is due to occasional pre-monsoon rains in those months which occurs in every year.

study is only upto April) which was probably due to a change in the mode of administration of the drugs. In 1965-66 INH and thioacetazone was given in a single dose in the morning whereas in 1967/68 (and also in 1969) it was given in two divided doses after meals. This is in conformity with the experience of others (6, 10).

For the purposes of this study, the year can be divided into two periods :

1. Period of no or minimum toxicity from August to January.

2. Period of maximum toxicity from February to July.

In the first period, temperature is comparatively low and humidity high in August, September and October and low in November, December and January. In the second period, temperature is high and humidity low. It therefore appears that a combination of high temperature and low humidity is associated with toxic reactions to thioacetazone.

Details of the various toxic reactions is shown in Table 2, in relation to seasonal variation in the following groups :—

1. Reactions having relationship with the season.
2. Reactions having no relationship with the season.

There were two cases of intractable vomiting, of seasonal relationship, for which drugs were withdrawn.

### Discussion

From the above findings, there appears to be some relationship between thioacetazone toxicity and atmospheric conditions. It has been observed that most of the toxic reactions are gastrointestinal (1,4,7, 9, 10) and maximum number occur in one particular period of the year viz February to July. Factors which may influence the incidence of toxic reactions may be enumerated as follows :

1. Under-nourished condition of the patient leading to low body resistance.
2. Some kind of minor Electrolyte imbalance in the body, due to high excretion of salt and water through perspiration.
3. Low excretion of the drug through the kidney due to increased perspiration.
4. High concentration of the drug in the liver causing derangement of liver function, which is again due to low excretion of the drug through kidney.
5. Mucosal change in the gastrointestinal system making it more vulnerable to the untoward effects of the drug locally.

Atmospheric temperature and humidity in a particular geographical area are beyond our control. Whether and to what extent they are instrumental in influencing toxic reactions

requires careful study ; especially the inter-relationship, if any, of above mentioned factors with atmospheric data. The object of this preliminary report is to bring this interesting observation to the notice of other workers, with more facilities at their disposal, so that the association, if any between thioacetazone toxicity and seasonal variations could be properly investigated.

### Summary

Relationship between toxicity to thioacetazone and atmospheric temperature and humidity has been studied from 1965 to 1969. It is found that 89.70% of common toxic reactions to this drug occur from February to July.

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