A PRELIMINARY STUDY OF THE THERAPEUTIC EFFECTS OF 'VADRINE' IN LEPROSY

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Vadrine is a new Anti-Leprosy drug with the chemical name of 2-PYRIDYL-(4)-1,3,4-OXDIAZOLON-(5) p-AMINO-SALICYL-ATE, the following chemical formula :

2-Pyridyl-(4)-1,3,4-oxdiazolone-(5)-p-aminosalicylate

Its tuberculostatic activity was tested by BRODHAGE and SMITH as early as July, 1955 *in vitro* and *in vivo* and was found to be equal to that INH with much lower toxicity in guinea pig tests.

It has been tried as well reported on from Britain and from Rhodesia by JOPLING and RIDLEY and ALLAN. In another report BRECHET says that Vadrine has advantages in its rapid action in the first 12 to 18 months, its lack of toxicity and side effects and its reactions are at a minimum; when tried alone it was found to develop drug resistance after about a year by JOPLING. BRODHAGE has tested this drug on animals, particularly rats, along with DDS on murine leprosy, experimentally introduced into the testes. He has reported that both the drugs singly have very little effect on the bacilli, while together they inhibit the increase of mycobacteria to a marked degree. In murine leprosy, he says, Vadrine is superior to DDS.

As far as is known this drug has not been tried in India. Ten thousand tablets of 400 mgm. each of Vadrine were placed at our disposal by Ed. Geistlich Sons, Chemical Works, Switzerland, for trial at this leprosarium in May last year. It was decided to try its effects on patients having nasal, ocular and laryngeal lesions in conjunction with the usual dosage of 600 mgm. per week of DDS. The dosage selected for this preliminary report of Vadrine was

10 mgm. per kg. of body weight three times a day, i.e. 30 mgm. per kg. of body weight daily.

This treatment was started on 11 patients after complete examination of nose, eyes and larynx and also general examination to exclude any other disease accompanying leprosy. The treatment was continued for 3 months.

No controls were studied as these patients had been steadily getting worse in spite of the full dosage of DDS for the last 6 months and nothing else did any good to their nasal, ocular and laryngeal leprosy.

The greatest effect of this three monthly experiment was seen in nasal leprosy, the results of which were recorded in 11 patients as 'good' or 'very good', both clinically or bacterially; the bacterial index was negative in 1 case in the nose, and 1 or less than 1 in all others, after an initial bacterial index in the nose of 6, 5 or 4.

Very little effect was seen on ocular and laryngeal leprosy. At the end of three months the nasal smears were again taken and showed a marked improvement in bacillary index. The bacilli in most of the cases appeared in broken forms which are considered to be non viable bacilli according to the latest view. In some cases the nose became free of leprosy bacilli, which considering the fact that generally it is the last part to be free, is remarkable.

In the natural progress of the disease in the nose, the first microscopic change noticed is the general swelling of the cartilaginous parts. In this series case No. 6 Shri Guru Pado was a patient of this type. His nose became free of leprosy bacilli at the end of 3 months and the swelling disappeared leaving no deformity at all, thus avoiding the ugly deformed nose which would have appeared in the ordinary course of leprosy treatment with DDS.

No resistance to the drug developed during this period in any patient. It is proposed to restart the treatment after a rest period of 2 months.

Reactions

Reaction appeared in 4 cases out of 11 ranging from mild itching on the face and other parts of the body to severe erythema nodosum leprosum, high fever, inflammation of the lepomatous lesions, and ulceration. Only in one case No. 10, which was severe, was the treatment stopped. In this case treatment had to be stopped completely not only with Vadrine but also with DDS. The reaction came on the 51st day of the treatment. The reaction was brought under control after 18 days but Vadrine was not given again because of fear of bringing on another reaction. The patient was put on hydnocarpus oil injections. The nose condition in this case became worse and the bacterial index during the reaction increased but at the end of the reaction it decreased markedly again. In the other cases

the ulceration of the nose responded by slight improvement to complete healing. The cases which had already developed nose deformity had symptoms connected with the deformity, and did not improve and required surgical treatment.

Other cases of ulcers which were positive for leprosy bacilli were also improved and the ulcers healed. There was no effect on trophic ulcers infected with secondary organisms.

Summary

Vadrine 30 mgm. per kg. per day with 600 mgm. weekly of DDS was tried on 11 patients having nasal, ocular and laryngeal complications for 3 months. The drug had a very good effect on the whole on nasal complications, but slight or no effect on other complications.

Severe reaction was noted only in one case out of eleven.

Conclusion

Vadrine in conjunction with the usual dosage of DDS has an accelerating effect and makes the patients free from *Mycobacterium leprae*, especially in the nose, during the first three months of treatment.

References

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