A Report on the Use of Carbarsone in Pulmonary Tuberculosis*

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Carbarsone is an arsenic compound and has been used for a number of years in the treatment of amebic dysentery. It is the trade name for p-carbamino phenyl-arsionic acid (H₂O:As.C₆H₄NHCONH₂) which was first prepared by Ehrlich. It is a white, crystalline, odorless solid, stable in air, with a slightly acid taste, and is practically insoluble in water, but is soluble in carbonate or bicarbonate solutions.

Our interest in the use of carbarsone in the treatment of tuberculosis was stimulated by the work of Dr. Robert Silver of Baltimore, Maryland, who had been using carbasone in the treatment of various forms of the disease. His results were far from conclusive, but several patients were apparently improved, and in February 1950 before a Regional Meeting of the American College of Physicians, he reported that the drug had a retarding effect on experimental tuberculosis in guinea pigs as well as in human tuberculosis. We, therefore, decided to try carbarsone on a limited number of patients at Eudowood Sanatorium to determine whether this drug had any effect on clinical tuberculosis. The therapeutic program was the same as that outlined by Dr. Silver and was continued for a period of at least three months. This therapy consisted of:

1. Carbarsone 3¾ grains—twice daily for five days.
2. Sulfadiazine 7½ grains—four times a day for five days.
3. Ten days rest without medication.
4. Carbarsone 3¾ grains—twice daily and sulfadiazine 7½ grains—four times daily for five days in combination, followed by ten days rest.

This last medication was repeated over and over during the entire therapeutic trial.

Before treatment the following procedures were carried out, complete blood count, sedimentation rate and sputum examinations, including sensitivity of organisms to streptomycin when streptomycin had been used previously. These were repeated at six week intervals. X-ray films were taken before treatment and at 30 day intervals thereafter. The clinical condition of the patient was checked at two week intervals, particularly concerning cough, expectoration, weight, etc.

Clinical Trial of Carbarsone on Pulmonary Tuberculosis

Thirty patients with pulmonary tuberculosis were placed on carbarsone therapy for a period of at least three months and several as long as six months. The cases treated were classified as predominately exudative or productive. Practically all cases were far advanced with a poor prognosis so that no unusual results were anticipated, but it was our desire to observe

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any tendency toward improvement in order to determine whether further and more extensive clinical trials would be advisable. Cases were divided into predominately exudative and predominately productive lesions.

**Cases with predominately exudative lesions:**

There were only three cases which might be classified as exudative. One had a pneumatic involvement which showed some clearing of disease and improvement, one was stationary and one had an acute exacerbation while on carbarsone. This latter case was treated with carbarsone before admission to the sanatorium.

**Cases with predominately productive lesions:**

Ten were worse, 16 were stationary and one was improved. Of those that were worse, five had streptomycin and para aminosalicylic acid after discontinuing carbarsone—all of these cases were improved on streptomycin and para aminosalicylic acid therapy.

Only one case of tuberculosis of the kidneys received carbarsone for two months. At the end of this trial period, the patient was unimproved clinically. This patient was placed on streptomycin and para aminosalicylic acid after discontinuing carbarsone, and showed considerable symptomatic improvement after two months treatment.

**Results**

There were only two patients of the entire group who seemed to be improved while on carbarsone, but this improvement was far from impressive. The rest were either stationary or worse. The group studied was too small to form any conclusion, but it was our impression that in these cases the disease seemed to run its natural course without any beneficial effects noted. Several who received carbarsone before any other antibiotic, were either stationary or worse, whereas, these same patients unmistakably improved when placed on streptomycin and para aminosalicylic acid.

**X-Ray Analysis**

From the x-ray film appearance 14 were considered stationary, 14 worse, one slightly improved and one moderately improved while on carbarsone.

Of the entire group only two patients felt generally better, but there was no evidence of improvement in x-ray film or laboratory findings.

There was no toxic manifestation noted except a skin rash in one patient, and it was doubtful if this was due to the medication. The drug was discontinued because she had received it for over three months and had done poorly. She died several weeks later.

There seemed to be a tendency in about one-half of the patients to have an increase in cough and expectoration for several weeks after the drug was begun, and thereafter they continued at the pretreatment level. Only one had conversion of sputum from positive to negative during the course of treatment.

Seven showed gain in weight of from two to 14 pounds, while 16 lost from one to eight pounds and six maintained their weight.
In all patients with fever, little or no change in temperature took place. In one, there was an elevation to 103 degrees F., due to acute exacerbation of the disease while still on the drug.

There was no change in the hemoglobin, red blood count or white blood count in any case.

Two patients showed improvement in sedimentation rate “Cutler method” (a drop of 5 mm. per hour). Six were worse (an increase of 5 mm. or more per hour). Twenty-one were stationary.

Resistance to streptomycin: There was no change in sensitivity to tubercle bacilli to streptomycin in several patients on whom streptomycin sensitivity tests were run before and after carbarsone therapy.

**Case Report**

The following is an example of the Predominately Exudative Type:

Carbarsone—From March 21, 1950 to August 11, 1950.

This patient, W.P., a 49 year old, white male, was admitted to Eudowood Sanatorium February 9, 1950. Onset, with fatigue and loss of weight of two years duration. X-ray film, one month before admission, revealed evidence of disease which proved to be active pulmonary tuberculosis. On admission, he had an area of consolidation in the right lung above the third rib. His temperature was 100 degrees F. Sputum positive for tubercle bacilli. He was started on streptomycin (one-half gram twice a day) February 10, 1950, and discontinued May 8, 1950. His temperature had gradually come down to 99.2 degrees F., but this change occurred before carbarsone therapy. He has gained 14 pounds in weight while on carbarsone, and the disease has gradually cleared although he still has a positive sputum. His sedimentation rate has dropped from 26 before therapy, to 18 at the end of carbarsone. He has improved about as one would have expected from his streptomycin therapy and bed rest. There has been no additional improvement that one could attribute to carbarsone. Surgery is being contemplated.

Since concluding our clinical observation on carbarsone, we have received a report from Dr. J. W. Frost of the Lilly Research Laboratories on carbarsone therapy in human and animal experiments. He states that...
several patients studied at the Lilly Laboratories for Clinical Research, showed no clinical response, and, likewise, animal work showed evidence that the material did not have any effect on experimental tuberculosis in mice or guinea pigs.

SUMMARY

Clinical observations on 30 cases on carbarsone showed no evidence of any effect of this drug on pulmonary tuberculosis or one case of renal tuberculosis. Unless evidence can be obtained to show a retarding effect of carbarsone on experimental tuberculosis further clinical trials are not warranted in our opinion.

RESUMEN

Las observaciones clínicas en 30 casos tratados con carbarzona no mostraron evidencia alguna de efecto sobre la tuberculosis pulmonar ni tampoco en un caso de tuberculosis renal. A menos que se obtenga evidencia de un efecto retardante de la carbarzona en la tuberculosis experimental, no estan justificados nuevos ensayos clínicos en nuestra opinión.

RESUME

Les observations cliniques de 30 malades traités par le carbazone n'ont montré aucun effet net sur la tuberculose pulmonaire et dans un cas sur une localisation rénale. Ce n'est que si les travaux expérimentaux permettent d'obtenir un effet retardant sur l'évolution de la tuberculose que de nouveaux essais cliniques avec ce produit se montreraient nécessaires.