Oxyphenbutazone (Tanderil, Geigy) is well known as an anti-inflammatory agent, and reports on its usefulness in chronic rheumatic conditions, in most branches of surgery, and in obstetrics and gynaecology, have appeared in recent years. Though closely related to phenylbutazone, it is said to have fewer side-effects.

It has become increasingly clear that there is a place for anti-inflammatory drugs in the therapy of pulmonary tuberculosis. Extensive trials have been done on the corticosteroids being used in this condition, as 'life-savers', to lessen pulmonary fibrosis, to speed resorption of pleural effusion, etc., but their potential dangers have become deterrents to us except in the special cases of tuberculous meningitis, effusion, and recently developed bronchogenic disease. Similarly, the newer proteolytic enzymes have been tried because of their ability to free sputum and improve ventilation. It was therefore decided to conduct a small clinical trial of Oxyphenbutazone in this mission hospital, in the hope that it might improve the sense of well-being in the depressed Africans whose lives are greatly affected by the verdict of years of treatment, probably without work; also that it might lessen cavity formation and lung scarring and aid the entrance of the tuberculostatics into the affected lung tissues. A secondary aim was to speed the treatment so as to release beds quicker for the never-ending number of people needing hospitalization and to improve their condition so rapidly that even the lesser educated ones would be willing to remain here for the necessary time.

Mode of Action
Miller et al., examined the inflammatory process, postulated that macromolecular proteins, such as fibrin, form in the tissue spaces in response to the primary injury. It is presumed that plasmin, capable of digesting such fibrin, cannot act because of some inhibitor, as yet not isolated. The hydrophilic fibrin causes swelling of the affected part with resultant capillary stasis and clot formation. Carbon dioxide builds up in the tissues, while oxygen, antibodies and antibacterial agents are kept out. Probably the proteolytic enzymes release the plasmin capable of digesting the fibrin, while the drug under review, Oxyphenbutazone, competes with the inhibitor, thus permitting the plasmin to work. It is certainly not a proteolytic enzyme, and it is quite unrelated to the corticosteroids.

METHOD AND MATERIAL
The 50 patients selected for the trial were proved to have pulmonary tuberculosis clinically, radiologically, and by microscopic sputum examination, and they were only used in the trial if they were considered suitable patients to receive the 'first-line' drugs, namely streptomycin, neotize and PAS. If any other tuberculostatics were thought necessary, the patients were excluded. Twenty-five were given the trial drug, the others receiving a placebo. No member of the nursing or laboratory staff was told the name or nature of the drugs until the completion of the trial. All routine drugs were prescribed in the usual dosage for the age and weight of the patient and, in addition, Tab.

Ferrous Sulph. Co.BPC was ordered when hypochromic anaemia was found. A high-protein diet was always given, often with protein casilate added, and supplemented in all cases with vitamins. Bed rest was strictly enforced for all patients involved in the trial.

The Oxyphenbutazone was given as 2 tablets i.d.s. in the first 2 weeks followed by 1 tab. i.d.s. thereafter, until the completion of 2 months.

Chest X-rays were taken on admission and monthly, read by one doctor only, who was experienced in interpreting such films. The result was recorded as 'excellent' when gross signs of exudative disease or numerous soft-walled cavities had cleared within the 2 months. ‘Good’ was taken to mean definite improvement though signs of active disease persisted, while ‘poor’ signified little or no improvement at all radiologically.

Sputum was examined microscopically on admission and at monthly intervals, and bacilli were counted by Gaffky's method. An 'excellent' result was reported if the sputum count, previously as high as 8 or 9, was negative by the end of the 2 months, and if no bacilli were seen during intensive searching. A 'good' result indicated a definite lessening of the bacilli count, while 'poor' was applied to those cases with no change whatsoever.

The ESR was also assessed monthly as an index of the inflammatory process. Similar criteria were laid down, namely, 'excellent' when there was a fall from very high levels (as high as 100 mm./hour) to normal; 'good' when a substantial drop occurred, but not to normal levels; and 'poor' when there was no change at all.

Finally the patients' weights were recorded weekly and a full record kept of all subjective reports on sweating, depression, possible side-effects, etc.

RESULTS
It will be observed from Tables I - IV that, of the patients receiving the trial drug, 11 showed an excellent X-ray response compared with 6 on the placebo, while fewer had a poor result. The sputum results showed little difference

### TABLE I. RADIOLOGICAL CHANGES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>Excellent</th>
<th>Good</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxyphenbutazone</td>
<td>25</td>
<td>11</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Placebo</td>
<td>25</td>
<td>6</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>

### TABLE II. SPUTUM BACILLI COUNTS (GAFFKY)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>Excellent</th>
<th>Good</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxyphenbutazone</td>
<td>25</td>
<td>3</td>
<td>15</td>
<td>7</td>
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<tr>
<td>Placebo</td>
<td>25</td>
<td>4</td>
<td>12</td>
<td>9</td>
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</tbody>
</table>

### TABLE III. ESR CHANGES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>Excellent</th>
<th>Good</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxyphenbutazone</td>
<td>25</td>
<td>13</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Placebo</td>
<td>25</td>
<td>9</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>

### TABLE IV. WEIGHT CHANGES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>Period</th>
<th>Average weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxyphenbutazone</td>
<td>25</td>
<td>8 weeks</td>
<td>11 lb.</td>
</tr>
<tr>
<td>Placebo</td>
<td>25</td>
<td>8 weeks</td>
<td>7 lb.</td>
</tr>
</tbody>
</table>
between the groups. The ESR results were deemed excellent in 13 of the trialists, compared with only 9 on the placebo; and substantial weight gain was also noticed in those receiving the Oxyphenbutazone. It might be noted here that the latter drug was given to 7 patients with gross fibrotic disease of long standing whose weight never changed and in whom there was little radiological improvement. Thus the average gain of 11 lb. in 8 weeks occurred actually in 18 patients only, some of whom gained more than 20 lb. in weight.

Clinically it was remarked by the nursing sisters that the temperatures of those on the trial drug dropped to normal within 3 days of the commencement of treatment, compared with the usual slow decline in temperature in the others. The nurses reported, at the end of the trial and before the nature of the drugs was disclosed, that all patients receiving Oxyphenbutazone spoke of easier expectation (possibly accounting for the continued presence of many bacilli shown above), and a definite sense of well-being with fewer complaints of chest pains, anorexia and apathy.

Side-Effects

Except for one patient developing stomatitis on the drug, no side-effects were observed, even though the drug was administered to patients with a history of cardiac disease, gastric upset and, in one case, allergy. No leucopenia was observed.

CONCLUSIONS

A controlled study comparing Oxyphenbutazone (Tanderil) and an inert placebo was conducted on 50 patients with active pulmonary tuberculosis.

It is probably wrong to attempt to draw too many conclusions from such a small trial, but it would appear that the claims made for the anti-inflammatory effects of Oxyphenbutazone are worth investigating further in pulmonary tuberculosis, particularly in those patients with a rapidly developing exudative type of pathology and a clinical picture of extreme cachexia. I was impressed with the marked subjective improvement in the Africans receiving Tanderil, and have no doubt that it aided their speedier recovery and earlier hospital discharge.

SUMMARY

The results are published of a small controlled trial of the anti-inflammatory drug. Oxyphenbutazone, in pulmonary tuberculosis in African patients. Clinical and radiological improvement with a fall in ESR were better in the Tanderil-treated group as compared with the placebo series. Its value in speeding the treatment and gaining the cooperation of such patients is noted and the need for a fuller trial stressed.

I wish to acknowledge my indebtedness to Dr. Dudley Jacobs of Pharmakers (Pty) Ltd. for both supplying the Tanderil (Oxyphenbutazone) for the trial and for his constant interest and encouragement.

REFERENCES