The Treatment of Tuberculous Pericarditis

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Twenty-seven patients with clinically primary tuberculous pericarditis were treated with prolonged chemotherapy consisting of intermittent doses of streptomycin and daily doses of para-aminosalicylic acid or isoniazid. Twenty-one patients did well and were symptom-free six months to three years later. Five, one of whom died, developed constrictive pericarditis. Another died of widely disseminated tuberculosis.

During the past four years we have treated 27 cases of clinically primary tuberculous pericarditis. By clinically primary we mean that the signs and symptoms were due to pericarditis and that no other active lesions could be demonstrated clinically at the onset of their illness.

All but two patients were males, the age ranged from 18 to 60. All but five were less than 30 years of age. The age and sex incidence merely reflects the age and sex incidence of our patient population. Sixteen or 59 per cent were Negroes which is significant in view of the fact that Negroes constitute only about 10 per cent of the Armed Forces.

Diagnosis

The etiology was proved in 13 by culture or by demonstrating the organism in tissues removed at operation or autopsy. A presumptive diagnosis was made in four patients by demonstrating a greatly thickened, shaggy pericardium by injecting air into the pericardial sac after the aspiration of fluid. The other 10 patients were diagnosed on clinical grounds, that is, by the presence of a typical, prolonged, severe, febrile illness in a young male, especially a Negro, with a positive Mantoux test, who responds promptly to streptomycin and para-aminosalicylic acid (PAS) or isoniazid (INH), but fails to respond to other therapy and in whom all other causes of pericarditis have been excluded.

TREATMENT

Treatment has consisted of bedrest, aspiration for diagnosis and/or relief of tamponade, and chemotherapy. Initially, chemotherapy consisted of streptomycin, 1 Gm. per day. After Deyke1 showed that intermittent therapy decreased toxicity and delayed the emergence of bacterial resistance, we changed our schedule to 2 Gm. every third day. After it had been shown that para-aminosalicylic acid, added to streptomycin, still further inhibited bacterial resistance and that the two drugs were synergistic,2 we incorporated the daily administration of 12 Gm. of this substance in our therapeutic regimen. Recently we have substituted isoniazid, 300 mg. daily for the para-aminosalicylic acid. In keeping with the recent trend toward treating minimal tuberculous lesions by prolonged periods of chemotherapy, we have also prolonged the duration of our treatment. Every patient should receive a minimum of 120 days of drug therapy; probably 8 to 12 months is the optimum period. The actual duration of therapy will depend upon the response of the patient, but must be continued for at least 90 days, preferably six months, after all signs of activity have ceased. Our criteria for inactivity are: (1) that the patient is afebrile; (2) that he has a normal sedimentation rate; (3) that there is no evidence of congestion; (4) that he has a normal sized heart with normal pulsations; and (5) that he has a stable, but not necessarily normal, electrocardiogram. After the completion of chemotherapy the patient is slowly, but progressively, ambulated. All of our patients have been hospitalized for at least one year. The duration of treatment has varied

From the Medical Services, Fitzsimmons Army Hospital, Denver, Colo., and U. S. Army Hospital, Camp Carson, Colo.
and is shown in table 1. Several patients received their initial treatment in other hospitals. Two patients have been previously reported.3

**RESULTS**

Chemotherapy was successful in 78 per cent of the entire series and in 69 per cent of the proved cases. Twenty-one patients have done well. They were completely asymptomatic when last seen, and fulfilled all our criteria for an inactive process. The follow-up period has varied from six months to three years after the conclusion of chemotherapy. Six patients were considered treatment failures in that five of them developed constricive pericarditis. One of these died following surgery, three have undergone successful pericardietomies, and one refused operation. There was one other death, a young Negro who died of widely disseminated tuberculosis six weeks after, the onset of his illness and after only 12 days of chemotherapy.

In analyzing the probable causes of failure, the most constant features were delay in treatment and inadequate dosage. Four of our failures received no chemotherapy until 3 to 11 months after the onset of their disease and all four developed constricive pericarditis. Another received inadequate therapy in that he received only 1 Gm. of streptomycin twice a week and 10 Gm. of para-aminosalicylic acid daily for only 90 days. At the conclusion of chemotherapy he had already developed constricive pericarditis. Figure 1 shows graphically the course in one of our patients who underwent prolonged treatment with a good result. Initially he was acutely ill with high fever, elevated venous pressure and a large effusion. Figures 2 and 3 show his chest x-ray films prior to and at the conclusion of chemotherapy. Figure 4 depicts the course in a patient with a poor result where treatment was delayed. His disease progressed and after he had developed constricive pericarditis he was started on streptomycin and para-aminosalicylic acid. The wide fluctuations in weight were produced by mercurial diuretics, thoracenteses, and paracenteses, the latter indicated by black arrows.

![Fig. 1. Condensed graph of a successful case showing temperature, venous pressure, heart size, erythrocytic sedimentation rate and treatment. PCN = penicillin. SM = streptomycin. PAS = para-aminosalicylic acid. INH = isoniazid.](http://circ.ahajournals.org/content/240/2/210.full)

![Table 1.—Chemotherapy](http://circ.ahajournals.org/content/240/2/210.full)

<table>
<thead>
<tr>
<th>Duration</th>
<th>Streptomycin</th>
<th>PAS</th>
<th>*INH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose &amp;amdash;</td>
<td>Dose &amp;amdash;</td>
<td>Dose &amp;amdash;</td>
</tr>
<tr>
<td>Gm.</td>
<td>qld</td>
<td>Grm.</td>
<td>Daily</td>
</tr>
<tr>
<td>Varying</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>60 days</td>
<td>1</td>
<td>✓</td>
<td>3</td>
</tr>
<tr>
<td>90 days</td>
<td>1</td>
<td>✓</td>
<td>3</td>
</tr>
<tr>
<td>120 days</td>
<td>2</td>
<td>✓</td>
<td>13</td>
</tr>
<tr>
<td>180 days</td>
<td>2</td>
<td>✓</td>
<td>3</td>
</tr>
<tr>
<td>210 days</td>
<td>2</td>
<td>✓</td>
<td>3</td>
</tr>
<tr>
<td>240 days</td>
<td>2</td>
<td>✓</td>
<td>2</td>
</tr>
<tr>
<td>Totals</td>
<td>27</td>
<td>100</td>
<td>24</td>
</tr>
</tbody>
</table>

* I.N.H. Varied from 30–120 Days.
He died the day after surgery. Figure 5 is his initial chest film with a massive pericardial effusion and Figure 6 is the chest film taken one month before death, which shows the greatly thickened, shaggy pericardium on contrast radiography.

The following factors are those we found most helpful in evaluating the course of their disease: (1) the duration of fever; (2) the duration of the pericardial effusion; (3) the progress of the electrocardiogram and (4) the evolution of congestion. The pertinent points of these factors are shown in tables 2, 3 and 4.

The most important factor in evaluating the result of therapy appeared to be the evolution of congestion. All of our successful cases lost all signs of congestion, but three of our failures had persistent congestion and the other three showed progressive congestion in spite of chemotherapy. Four of our cases have developed full-blown constrictive pericarditis within six months of the onset of their illness and this occurred within three months in two patients. Three had definite constrictive pericarditis when therapy was initiated.

Previous authors have pointed out that the mortality rate is much higher in those cases that are proved bacteriologically. In our series, the overall mortality rate was 8 per cent. Both fatal cases were proved by culture and autopsy. The mortality rate in the proven cases was 15 per cent. This appears to be a significant reduction in the anticipated mortality rate in this disease which is complex and which has a highly variable clinical course. Any evaluation of therapy should await a more prolonged
FIG. 5 (left). X-ray film of chest of patient shown in figure 4 with a large pericardial effusion.

FIG. 6 (right). X-ray film of chest of same patient one month before death. Air has been injected into the pericardial sac.

Table 2.—Duration of Fever

<table>
<thead>
<tr>
<th>Duration</th>
<th>Successful</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 30 days</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>14–30 days</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Less than 14 days</td>
<td>14</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3.—Duration of Effusion

<table>
<thead>
<tr>
<th>Duration</th>
<th>Successful</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>6–4 months</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>3 months</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>2 months</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>1 month</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Never definitely present</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 4.—Electrocardiogram

<table>
<thead>
<tr>
<th>Electrocardiogram</th>
<th>Successful</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remained abnormal</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Returned to normal</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Always normal</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Follow-up and final conclusions must be deferred until this has been accomplished.

Discussion

Our experience leads us to believe that every case of pericarditis should be studied exhaustively in an attempt to establish the etiology. Diagnostic studies should include pericardial aspiration with culture and/or guinea pig inoculation of the fluid obtained, contrast radiography, and, as a last resort, pericardial biopsy if necessary. We further believe that, when the diagnosis of tuberculous pericarditis is reasonably certain on clinical grounds, treatment should be instituted as soon as the initial studies have been accomplished, and not withheld pending the results of cultural studies or animal inoculations. Six weeks of chemotherapy with intermittent streptomycin and para-aminosalicylic acid or isoniazid is a benign form of treatment. In the event that the diagnosis ultimately proves to be erroneous, no harm has been done and if the diagnosis is later confirmed, valuable time has been gained.

If the patient fails to respond to treatment in spite of adequate medical management, in
that signs of congestion persist or progress, he
should be subjected to prompt surgical re-
section even though active disease is present. It
has been conclusively shown that surgical re-
section can be carried out even in the presence
of active disease without danger of dissemina-
tion.\textsuperscript{6-9} Chemotherapy should be continued
throughout the operative period and for at
least 90 days, preferably for six months, after
attaining an inactive stage.

**SUMMARY AND CONCLUSIONS**

1. Twenty-seven patients with clinically
primary tuberculous pericarditis were treated
with intermittent streptomycin and para-
aminosalicilic acid (PAS) or isoniazid (INH).

2. The outcome was considered successful in
21 and unsatisfactory in six patients. Con-
strictive pericarditis developed in five; one
died following surgery, and another of an over-
whelming tuberculous infection.

3. The total mortality rate was 8 per cent;
in the bacteriologically proven cases it was 15
per cent.

4. Chemotherapy should be initiated early
and should include streptomycin, 2 Gm. every
third day, and para-aminosalicylic acid, 12
Gm. daily, or isoniazid, 300 mg. daily, and
should be continued for at least six months
after all signs of activity have ceased.

5. Cases showing persistent or progressive
congestion in spite of adequate medical man-
agement should be subjected to surgery plus
chemotherapy even though active disease is
present.

**SUMARIO Español**

Veinte y siete pacientes con pericarditis
tuberculosa clinicamente primaria fueron trata-
dos con quimioterapia prolongada consistiendo
en dosis intermitentes de estreptomicina y
dosis diarias de acido paramino-salicilico o
isoniazid. Veinte y un pacientes mejoraron y
estuvieron libres de sintomas de seis meses a
tres años más tarde. Cinco desarrollaron per-
carditis constrictiva, uno de los cuales murió.
Otro murió con tuberculosis disseminada.

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The Treatment of Tuberculous Pericarditis
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Circulation. 1954;9:17-21
doi: 10.1161/01.CIR.9.1.17
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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