

## Adjunctive steroids for reducing residual pleural effusion in patients with TB

### CITATION

Fleishman SI, Coetzee AM, Mindel S, Berjak J, Lichter AI. Antituberculous therapy combined with adrenal steroids in the treatment of pleural effusions: a controlled therapeutic trial. *Lancet*. 1960 Jan 23;1:199-201

### RESEARCH QUESTION

Compared to standard therapy, how effective is adjunctive steroid therapy for treating patients with pleural effusion of unknown cause?

### THE STUDY

Controlled therapeutic trial.

### STUDY SETTING

Central hospital within the mining area of Witwatersrand, Johannesburg.

### PARTICIPANTS

Included: Mineworkers with pleural effusion of unknown cause, presumably all men.  
 Excluded: Patients with Pulmonary Tuberculosis (TB), other TB, adenopathy, abdominal masses, vitamin deficiency, bilateral effusions.

### INTERVENTIONS

1. *Treatment V*: Ascorbic Acid 500mg IM daily for 14 days
2. *Treatment P*: Procaine Penicillin 300,000 units IM twice daily for 14 days
3. *Treatment T*: ATT (see below)
4. *Treatment TS*: ATT plus corticosteroids (see below)

	Regular	ATT	ATT Plus
<b>Description</b>	<i>Streptomycin</i>	<i>INH</i>	<i>Prednisolone</i>
<b>Dosage</b>	1g IM	200mg orally	10mg orally, then 5 mg orally
<b>Frequency</b>	Daily	3 times/d	3 times daily, then 3 times daily for rest of 8 weeks
<b>Duration</b>	8 wks	8 weeks	for 2 days at higher dose, rest of 8 weeks at lower dose

Co-interventions: 1. 3 tablets Vit B co daily  
 2. Bedrest

### OUTCOMES

Primary: Reduction in the extent of pleural effusion  
 Secondary: Are scurvy and pneumonia involved in the pathogenesis of pleurisy?

**RISK OF BIAS** (Risk Scale: Low – Moderate – High)

### SELECTION BIAS: moderate to high

Previously prepared sealed instructions of treatment. As each case was admitted to the trial, hospital clerical staff drew one so that the treatment was allocated at random. Table 1: Appears to be balanced for Initial weights and Initial ESR. However no other parameters (e.g. demographics) are reported on. The ESR appears to be low for TB for which you would normally expect readings of around 40+ mm/hr.

**PERFORMANCE BIAS: low**

(ie: What else happened that may have affected the result?)

Patients not blinded - Not a problem since outcome is not affected by patient's performance.

Patients were confined to hospital – good compliance to therapy

Period of bed rest varied according to "patient's condition" – article did not clarify who made this judgement.

Initial aspiration of 20 ml of pleural fluid may affect first four weeks' score.

**DETECTION BIAS: low**

Pleural effusions were scored by a panel of 5 doctors who, according to the authors, were blinded to the patient's treatment. No indication that the laboratory staff was blinded.

However, it appears as if the panel were aware of the treatment given at the beginning of the trial since on page 200, column 2 – "this result became known only at the completion of his course of treatment" almost indicating that they would have changed the treatment had they known?

**ATTRITION BIAS:**

No intention to treat analysis performed.

	<b>P</b>	<b>V</b>	<b>ATT</b>	<b>ATT + S</b>	<b>Total</b>
Started	19	21	19	20	79
Completed	17	19	19	20	75
Assessed	16	18	19	20	73

**STUDY FINDINGS**

Significant reduction in the extent of the effusion in TS at 4 weeks

No significant reduction seen from 4 weeks to 8 weeks

**PRESENCE OF RESIDUAL FLUID (95% CI)**

	<b>Treatment</b>	<b>Event Rate</b>	<b>RRR</b>	<b>ARR</b>	<b>NNT</b>
4 weeks	TS	E 11/20 = 0.55	35%	0.29	4
	T	C 16/19 = 0.84	(2%; 67%)	(0.02; 0.57)	(2 – 52)
8 weeks	TS	E 8/20 = 0.40	49%	0.39	3
	T	C 15/19 = 0.79	(14%; 85%)	(0.11; 0.67)	(1 – 9)

**ADVERSE EVENTS**

Four patients deteriorated: Treatment change from V, P to T, TS

**COMMENTS**

Adjunctive steroid therapy appears to be an effective treatment for reducing residual pleural fluid in patients with pleural effusion of unknown cause.

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