- **Official Title of the study:**

  Liberation of Captive Pleura: Chemical Pleural Adhesiolysis Versus Mechanical Pleural Adhesiolysis in Stacked Pleural Effusion

- **NCT number:** Not Available Yet

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- **Investigators:** Hanan M. Shata (1), A. M. Abumossalam (2), Ahmed Abd-Elgawad Radi (2), Amir Soliman (3), Eman Shawky (4)
- **Institutional Affiliations:**
  - (1) Department of Chest Medicine, Faculty of Medicine, Damietta University, Damietta, Egypt
  - (2) Department of Chest Medicine, Faculty of Medicine, Mansoura University, Mansoura, Egypt
  - (3) Department of Public Health and Community Medicine, Faculty of Medicine, Delta University for Science and Technology, Gamasa, Egypt
  - (4) Department of Chest Medicine, Faculty of Medicine, Arish University, Arish, Egypt

- **Study Location:** Chest Medicine Department, Mansoura University Hospital
- **Trial Period:** March 26, 2026 to June 27 2026
- **Ethics Approval Code:** Institutional Research Ethics Committee, Mansoura University (Code: R.26.03.3607)

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1. Introduction & Rationale

Complicated parapneumonic pleural effusion (CPPE) remains an important cause of morbidity and may progress from exudative to fibrinopurulent and organizing stages characterized by intense pleural inflammation, fibrin deposition, septa formation, and restrictive pleural peel development

(1, 2). These pathological changes impair pleural drainage and hinder lung re-expansion, which represents the principal objective of effective therapy (3, 4).

Current management strategies rely on antimicrobial therapy and pleural drainage, often supplemented by intrapleural fibrinolytic therapy and /or surgical intervention (2). Although combined tissue plasminogen activator (tPA) and DNase therapy improves pleural drainage and clinical outcomes, their application remains limited in resource-con

Strained settings because of high cost, potential bleeding complications, repeated dosing requirements, and inconsistent availability (5, 6). Thoracoscopic mechanical pleurolysis/adhesiolysis provides direct vision-guided disruption of fibrinous septa and remains an effective intervention in selected patients with loculated pleural infection (7, 8). However, even when performed using medical thoracoscopy, the procedure requires specialized expertise, dedicated equipment, and procedural resources that may limit widespread accessibility in some healthcare settings (1, 2).

2. Study Objectives

- **Primary Objective:** To evaluate and compare the therapeutic efficacy of intrapleural 3% hydrogen peroxide, intrapleural corticosteroids (dexamethasone or triamcinolone), and standard medical thoracoscopic mechanical pleurolysis in managing complicated non-malignant pleural effusion.
- **Secondary Objective:** To assess treatment response through a novel composite clinical/radiological efficiency score incorporating lung volumetry, diaphragmatic excursion, pleural thickness, fluid volume drained, and effusion complexity.

3. Methodology

3.1. Study Design & Setting

- **Design:** Parallel-group, pilot randomized controlled clinical trial.
- **Setting:** Outpatient clinics, emergency services, and inpatient respiratory wards at Mansoura University Hospital.
- **Randomization:** 36 eligible patients randomized in a 1:1:1 ratio into three groups (12 patients per arm) using computer-generated block randomization with sequentially numbered sealed opaque envelopes.
- **Blinding:** Open-label for operators/participants due to procedural differences; single-blinded for radiological and ultrasonographic assessors.

3.2. Eligibility Criteria

Inclusion Criteria:

- Patients aged 18–62 years.
- Presence of unilateral complicated parapneumonic pleural effusion requiring pleurolytic intervention.

- Confirmed complicated effusion via imaging (loculation), biochemical criteria (pH < 7.2, glucose < 60 mg/dL), and/or microbiological criteria (positive Gram stain or culture).
- Histopathological exclusion of malignant and tuberculous pleural disease prior to enrollment.

Exclusion Criteria:

- Malignant or tuberculous pleural effusion.
- Transudative effusion.
- Frozen chest syndrome or chronic trapped lung.
- Pregnancy.
- Bleeding diathesis.
- Patient refusal to participate.

4. Intervention Protocols

Group A: Hydrogen Peroxide-Mediated Pleurolysis

- Administered via an existing intercostal drain after the initial drainage phase.
- Pharmaceutical-grade hydrogen peroxide is diluted with sterile saline to a 3% concentration.
- A total volume of 250–300 ml is instilled (accounting for tubing dead space to ensure 250 mL reaches the pleural cavity).
- The drain is clamped for 4–6 hours while the patient alternates between supine and lateral decubitus positions to aid intrapleural distribution.
- Drainage is then resumed, and a second session is repeated 24 hours later.

Group B: Steroid-Mediated Pleurolysis

- Administered via an existing intercostal drain.
- Agent used is either Dexamethasone 8 mg or Triamcinolone acetonide 0.3–0.6 mg/kg (approx. 80 mg), diluted in normal saline to a total volume of 250–300 mL.
- The drain is clamped for 4–6 hours with identical positional rotation protocols as Group A.
- A total of two sessions are conducted 24 hours apart.

Group C: Thoracoscopic Mechanical Pleurolysis

- Performed under local anesthesia and conscious sedation.
- Involves direct visualization of the pleural cavity, mechanical disruption of fibrinous septa/adhesions, evacuation of loculations, and placement of an intercostal drain.

5. Outcome Assessment & Endpoints

5.1. Baseline & Follow-up Assessments

- Assessments are conducted pre-intervention and at 7 days post-procedure.

- **CT Volumetry:** 128-slice multidetector CT scanner to quantify affected lung volume and percentage improvement.
- **Ultrasonography:** M-mode (2.5-MHz) for diaphragmatic excursion and B-mode (7-MHz) for fractional pleural thickness reduction across standardized zones.
- Effusion complexity classified sonographically as simple, complex, or septated.

5.2. Primary Endpoint (Composite Radiological Efficiency Score)

A 0–6 point composite score evaluates treatment efficiency at day 7, with a score of >= 5 defined as a treatment success. Points are awarded as follows:

- **Lung volumetric improvement:** >= 30% improvement = 1 point.
- **Diaphragmatic excursion improvement:** >= 30% improvement = 1 point.
- **Pleural thickness reduction:** >= 30% reduction = 1 point.
- **Drained pleural fluid volume:** >= 30% increase = 1 point.
- **Effusion complexity:** Septated = 0 points, Complex = 1 point, Simple = 2 points.

6. Statistical Analysis

- Data analyzed using SPSS version 27.
- Quantitative variables evaluated via paired t-test for within-group pre- and post-intervention changes.
- Between-group comparisons analyzed using one-way ANOVA followed by planned contrast analysis.
- Categorical variables analyzed using Fisher's exact test.
- Pearson correlation utilized to evaluate associations between the composite efficiency score and radiological parameters.
- Statistical significance set at $p < 0.05$.

7. Ethical Considerations

- The protocol conforms to the Declaration of Helsinki.
- Written informed consent obtained from all patients following a detailed explanation of procedures, risks, and benefits.
- All patient data is rigorously anonymized and securely stored.
- The study protocol was approved by the Institutional Research Ethics Committee, Mansoura University (Code: R.26.03.3607). The trial adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants after detailed explanation of the study procedures, possible risks, and expected benefits. All data were anonymized and stored securely to maintain patient confidentiality.
- Patients who failed chemical pleurolysis were offered crossover to mechanical pleurolysis as a rescue intervention; however, the primary analysis was conducted according to the originally allocated intervention groups.

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