The Use of Hypertonic Aerosol in Production of Sputum for Diagnosis of Tuberculosis*

Comparison with Gastric Specimens

NESTOR M. HENSLER, LT. COLONEL, USAF, MC,
CHARLES G. SPIVEY, JR., MAJOR, USAF, MC,
and TOM M. DEES, CAPTAIN, USAF, MC

Scott Air Force Base, Illinois

Although radiologic characteristics and tuberculin positivity are important, proof of the diagnosis of pulmonary tuberculosis depends upon demonstration of tubercle bacilli in bronchial secretions. Failure to recover tubercle bacilli may leave sufficient doubt of the validity of the diagnosis to diminish the physician’s vigor in pursuing and the patient’s willingness to accept treatment. When the patient is actively producing sputum or when disease is extensive, little difficulty is encountered. However, 30 per cent of the patients admitted to the diagnostic ward of our Tuberculosis Section are unable to produce adequate sputum for bacteriologic study. Many of these have minimal lesions and present diagnostic problems. Traditionally, the early morning gastric aspiration has been utilized in such cases, but even with multiple specimens, the diagnostic yield is low (less than 50 per cent).

Bickerman, Sproul and Barach described a method utilizing a heated hypertonic aerosol in obtaining sputum for cytologic diagnosis of lung cancer. They were able to collect adequate sputum specimens in a significant number of subjects without evidence of pulmonary disease and with no cough or sputum. This report suggested that similar methods might be of value in the bacteriologic diagnosis of tuberculosis and stimulated the present study.

Material

During the period of the study (May, 1959 - October, 1960), 171 male patients were admitted to the diagnostic ward of the Tuberculosis Section. Criteria for admission to the study were: (1) no previous bacteriologic diagnosis of tuberculosis and, (2) absence of spontaneous cough or sputum production. Fifty-two patients met these criteria, 13 of whom were eventually found to have either inactive disease or non-tuberculous lesions. The remaining 39 patients were diagnosed as having active tuberculosis and are the subject of this report. Extent of disease

<p>| TABLE 1—COMPARISON OF CULTURAL RESULTS OF INDUCED SPUTUM AND GASTRIC SPECIMENS (39 CASES OF TUBERCULOSIS) |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Type of Specimen</th>
<th>Number of Patients</th>
<th>Culture Positive</th>
<th>Total Specimens</th>
<th>Culture* Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric</td>
<td>37</td>
<td>16 (43 per cent)</td>
<td>108</td>
<td>30 (28 per cent)</td>
</tr>
<tr>
<td>Sputum</td>
<td>31</td>
<td>20 (65 per cent)</td>
<td>89</td>
<td>47 (53 per cent)</td>
</tr>
</tbody>
</table>

*Difference significant (p<.0002)

was minimal in 18, moderately advanced in 18, and far advanced in one. A patient with tuberculous pleurisy and one with renal disease, but without evidence of pulmonary disease, is also included.

**Methods**

A heated nebulizer which delivers a liquid and vapor mist at a temperature of approximately 105°F was used. A solution of 10 per cent sodium chloride in 20 per cent propylene glycol was nebulized either with oxygen at a flow rate of 7 liters per minute, or with an electric diaphragm air compressor as the propellant. The patient was instructed to inhale the aerosol mist from a distance of four to six inches from the outlet of the nebulizer. All material coughed up during and for one hour after a 20 minute period of nebulization was collected and this was repeated approximately four to six times during the day. The pooled specimen was submitted to the laboratory. In each case, gastric specimens were obtained on three successive days, followed by three successive days of induced sputum collection. Later in the study, the saline content of the solution was reduced to 5 per cent in an effort to avoid clogging of the jets of the nebulizer. A minimum of 5 cc. of total collected sputum was considered adequate. Cultures were processed by standard methods' and cultured in duplicate on Lowenstein-Jensen and Middlebrook 7H10 media.

**Results**

One or more adequate gastric specimens were obtained in 37 of the 39 patients, yielding positive cultures in 16 individuals (43 per cent). One or more adequate sputum specimens were obtained in 31 of these individuals with positive cultures in 20 cases (65 per cent). All together, a total of 108 gastric specimens were collected, 30 of which were positive on culture for *M. tuberculosis* (28 per cent). Of 89 sputum specimens, 47 yielded positive culture (53 per cent). (Table 1).

Direct comparison of induced sputums and gastric specimens in the same patient was not possible in all cases because of inability to obtain either adequate gastric specimens or to induce adequate sputum. However, 28 patients produced two or more adequate specimens by both methods. Thirteen of these 28 patients yielded positive cultures by both methods. In six individuals, positive induced sputum cultures were obtained, but all gastric specimens were negative, and in one individual, a single gastric specimen was positive and all sputum specimens were negative on culture. Thus, 19 patients (68 per cent) were bacteriologically positive for acid-fast bacilli by induced sputum, whereas only 14 patients (50 per cent) yielded one or more positive gastric specimens. In this group of paired specimen patients, 25 of 83 gastric specimens yielded tubercle bacilli

<table>
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<th>Positive*</th>
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</thead>
<tbody>
<tr>
<td>Gastric</td>
<td>14 (50 per cent)</td>
<td>83</td>
<td>25 (30 per cent)</td>
</tr>
<tr>
<td>Sputum</td>
<td>19 (68 per cent)</td>
<td>81</td>
<td>43 (53 per cent)</td>
</tr>
</tbody>
</table>

*Difference significant (p+.002)*
(30 per cent), whereas 43 of 81 induced sputum specimens yielded tubercle bacilli on culture (53 per cent) (Table 2). It is of additional interest that smears of sputum concentrate were positive for acid-fast bacilli in six individuals.

Discussion

It would seem logical that material collected directly from the bronchi would contain more viable organisms than would bronchial secretions which have traversed the bronchial tree, the hypopharynx, the esophagus, and have been diluted and digested by gastric juices, and it is generally conceded that sputum is superior to tracheal aspirate for bacteriologic study in suspected pulmonary tuberculosis. Some have contended that with careful indoctrination, all patients can be taught to produce sputum. While this is possible in many cases, the degree of success depends upon the zeal and enthusiasm of physician and attendants and upon the cooperation of the patient. Many such "forced" sputa are in reality saliva and of little value. Tracheal lavage and laryngeal swabs have met with some success, but in general have no advantage over gastric aspiration. Tracheal lavage requires experience and skill and the explosive cough produced is a hazard to the operator. Laryngeal swabs have not been found to be as adequate as gastric specimens. Bronchial washings at time of bronchoscopy and postbronchoscopic sputum will occasionally yield positive cultures, but obviously these techniques are not applicable as routine diagnostic measures.

Nebulization of isotonic solutions at room temperature produces aerosols which are 30 to 60 per cent humidity of saturated air at body temperature. By raising the temperature to 100-105°F, and by increasing the toxicity of the nebulized solution, it is possible to get aerosols which are at or above body humidity. At increased temperature, these jeta will hold more water vapor and the higher toxicity lowers the vapor pressure of the droplets, reducing their tendency to vaporize. These droplets are then carried to the lower respiratory tract where they are deposited. The hypertonic solution has a mildly irritating and an osmotic action in the smaller bronchi and bronchioles, producing cough and sputum. The warm aerosol does not have the irritant effect of a cold hypertonic aerosol on the pharynx and upper respiratory tract, and thus premature cough is avoided.

Barach, et al., and subsequently others have demonstrated that inhalation of hypertonic aerosol will yield adequate specimens for cytologic study in up to 86 per cent of subjects and in 54 per cent. Gas troscopic sputum were obtained in 45 (65 per cent). Most of the failures occurred early in the study, and although in a few cases poor patient cooperation may have played some role, inadequate instruction and inexperience was undoubtedly the major factor affecting success. Five failures occurred in the first ten patients admitted to the study, and only four in the subsequent 42. Patient acceptance has been excellent as compared to gastric lavage.

One question in our minds at the onset of the study was whether the composition of the aerosol would interfere with the ability of tubercle bacilli to grow out in culture. The relatively high percentage of positive cultures obtained indicates that the solution does not affect the viability of tubercle bacilli in the resultant sputum.

Some problems have been encountered in the use of apparatus. Frequent occlusion of the jeta resulted in maintenance problems. This was not greatly affected by reducing the concentration of saline to 8 per cent. Careful cleansing and flushing of the apparatus with alcohol after each use has minimized this problem. A greater problem has been short effective life of the heating elements, with delay in obtaining replacement parts. Clearly, a more durable element is needed to make the apparatus more serviceable.

From a diagnostic standpoint, induced sputa appear to be superior to gastric specimens in this group of patients. The series is small, however, and the increased numbers of patients with positive sputum diagnosis falls short of statistical significance. The relative percentages of sputum specimens versus gastric specimens yielding positive cultures reveal a significant superiority to the induced sputum (p< less than .002).

To date, only in-patients have been studied. Future study will be directed to comparison of a single-sitting collection of induced sputum with gastric cultures to determine the applicability of this technique to out-patient use.

SUMMARY AND CONCLUSIONS

Sputum induced by inhalation of a heated hypertonic aerosol yielded a greater number of cultures positive for tubercle bacilli than did gastric specimens from the same group of in-patients under investigation for tuberculosis. The method appears to have value in the diagnosis of inflammatory disease of the lung and deserves further study.

RESUMEN

El esputo provocado por la inhalación de un aerosol calentado hipertónico produjo un mayor número de cultivos positivos para el bacilo de la tuberculosis que los especi-
menes de contenido gastro en el mismo grupo de enfermos internados en los que se investigó tuberculosis. El método parece tener valor en el diagnóstico de enfermedad inflamatoria del pulmón y merece mayor estudio.

**RESUMÉ**

Des crachats provoqués par une inhalation d'un Aérosol hypertonique chaud donnent en plus grand nombre des cultures positives pour le bacille tuberculeux que les tubages gastriques dans un même groupe de malades hospitalisés en vue de préciser le diagnostic de tuberculose. Cette méthode paraît avoir de la valeur pour établir le diagnostic des infections pulmonaires et mériterait une étude plus poussée.

**ZUSAMMENFASSUNG**

Die durch Inhalation des erwärmten hypertonischen Aerosols bewirkte Sputumproduktion führt bei der Untersuchung auf Tuberkelbakterien zu einer grösseren Anzahl positiver Kulturen, als die Untersuchung des Magensaftes bei der gleichen stationär behandelten Patientengruppe. Die Methode erscheint wertvoll bei der Diagnose entzündlicher Lungenerkrankungen und verdient weitere Untersuchungen.

**REFERENCES**


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**ATRIAL INFARCTION OF HEART**

A clinical diagnosis of atrial infarction should be suspected in patients with ventricular myocardial infarction having any form of atrial arrhythmia. Frequent electrocardiograms should be obtained, especially if sinus rhythm has just been re-established after episodes of supraventricular tachycardia or atrial fibrillation.

The major electrocardiographic criteria for the diagnosis of atrial infarction are as follows: elevation of the P-Ta segment of over 0.5 mm. in V₃ and V₄ with reciprocal depression of the same segment in V₁ and V₂; elevation of the P-Ta segment of over 0.5 mm. in lead I and its depression in leads II or III; depression of the P-Ta segment of more than 1.5 mm. in precordial leads and 1.2 mm. in leads I, II, and III in the presence of any form of atrial arrhythmia.

The minor electrocardiographic criteria in making the diagnosis of atrial infarction are as follows: abnormal P waves: M-shaped, W-shaped, irregular or notched; depression of the P-Ta segment of small amplitude without elevation of this segment in other leads cannot be regarded by itself as positive evidence of atrial infarction.

A diagnosis of atrial infarction can sometimes be made when the presence of ventricular myocardial infarction cannot be definitely established by electrocardiogram.

The treatment of atrial infarction is similar to that of ventricular infarction. Attention should be directed to the control of atrial arrhythmias and to the prevention of mural thromb.