The Relative Efficacy of Spontaneous Sputa, Aerosol-Induced Sputa, and Gastric Aspirates in the Bacteriologic Diagnosis of Pulmonary Tuberculosis*

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There is no single test or combination of tests which is specific for the diagnosis of active tuberculosis except the cultural isolation of tubercle bacilli. Only a few of the disadvantages inherent in the absence of such confirmation are that both patient and physician may lack enthusiasm for prolonged and adequate chemotherapy, diagnostic surgery may be unavoidable, and contacts may go undetected and exposed to possible infection.

The *sine qua non* of success in obtaining bacteriologic confirmation of active pulmonary tuberculosis is the collection of adequate lung secretions. Two of the many available techniques for obtaining such material for culture, spontaneous sputum production and gastric aspiration, are almost universally employed. A third technique, induction of sputum by inhalation of a heated hypertonic aerosolized solution, has enjoyed increasing use. The purpose of this report is to compare the relative efficacy of these three methods and to assess their respective value in the bacteriologic diagnosis of pulmonary tuberculosis.

Methods and Materials

This report is concerned with a study of 225 adults with active pulmonary tuberculosis who were admitted to United States Air Force Hospital Scott between June, 1962 and June, 1964. Patients were classified as having minimal, moderately advanced or far advanced disease according to standard criteria. All subjects included in this series had either cultures positive for *Mycobacterium tuberculosis* or met satisfactory clinical criteria for active tuberculosis. The great majority were initial therapy patients. They were hospitalized until they had achieved either quiescent status or were transferred to a Veterans Administration hospital.

One hundred fifty-five patients who had not received antituberculosis chemotherapy of any type within one year of admission were considered separately. The remaining 70 patients who had received chemotherapy for a few days to several months immediately prior to admission constituted a second group. Both groups were comparable as to age and sex, but the treated group had a higher proportion of patients with advanced disease.

All patients with a productive cough submitted a minimum of three spontaneously produced specimens of sputum, each collected over a 24 hour period. Gastric aspirates and induced sputa were also obtained in a few instances. Those who were unable to produce at least three sputum specimens voluntarily had submitted to the laboratory a minimum of three fasting gastric aspirates and/or a minimum of three induced sputa. The latter were obtained by a modification of the technique of Bickerman, Sproul and Barach using a solution of 20 per cent propylene glycol and 10 per cent saline solution heated to 125°F. and aerosolized by a Puritan nebulizer with an electric diaphragm air compressor as the propellant. The aerosol was inhaled by the patient for 15 to 20 minutes four or five times daily, and all sputum collected over 24 hours by this technique was submitted as a single pooled specimen.

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Each specimen was processed in the laboratory by standard methods,3 planted in duplicate on both Lowenstein-Jensen and Middlebrook 7H10 media, incubated at 37°C for eight weeks and examined once weekly for growth. Classification as M. tuberculosis in each instance was made by typicality of colony morphology, demonstration of acid-fast organisms by the auramine technique, and a positive niacin test. Specimens showing no growth in all tubes at eight weeks were reported as negative.

RESULTS

Results in the group of 155 patients with active tuberculosis who had not received chemotherapy prior to admission are summarized in Table 1. Cultures of spontaneously produced sputa were positive in 70 of the 81 individuals (86 per cent) who had productive cough. Hence, in 45 per cent of the group, cultural confirmation of the diagnosis was accomplished from spontaneously produced sputa. Success by this method was a function of the severity of pulmonary involvement, being 77 per cent in those with far advanced, 44 per cent in those with moderately advanced, and only 32 per cent in those with minimal disease.

Cultures of aerosol-induced sputa and/or gastric aspirates were positive in 52 additional patients (34 per cent). Hence a total of 122 (79 per cent) had positive cultures. The increased yield with these additional techniques was most apparent in those patients with moderately advanced disease (42 per cent) and minimal disease (27 per cent), but even in those with far advanced disease there was a 23 per cent increase in the incidence of positive cultures.

A comparison of the efficiency of induced sputa and gastric aspirates is summarized in Table 2. In the entire group of 155 untreated patients, 194 gastric aspirates were obtained, of which 59 (30 per cent) were positive on culture. Of 344 induced sputa, 176 (51 per cent) were positive. This difference is statistically highly significant ($X^2=21.7$ p<0.001). When data from 72 bacteriologically proved patients are compared, these figures are 38 per cent and 69 per cent respectively, again a highly significant difference ($X^2=36.6$, p<0.001).

Table 2—Results of All Gastric Aspirate and Induced Sputum Cultures in 155 Untreated Tuberculous Patients

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number of Cases</th>
<th>Cases with Positive Cultures (Per Cent)</th>
<th>Cases with Positive Spontaneous Sputa (Per Cent)</th>
<th>Cases with Positive Induced Sputa and/or Gastric Aspirates (Per Cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal Tuberculosis</td>
<td>56</td>
<td>33 (59)</td>
<td>18 (32)</td>
<td>15 (27)</td>
</tr>
<tr>
<td>Moderate Advanced Tuberculosis</td>
<td>73</td>
<td>63 (86)</td>
<td>32 (44)</td>
<td>31 (42)</td>
</tr>
<tr>
<td>Far Advanced Tuberculosis</td>
<td>26</td>
<td>26 (100)</td>
<td>20 (77)</td>
<td>6 (23)</td>
</tr>
<tr>
<td>TOTALS</td>
<td>155</td>
<td>122 (79)</td>
<td>70 (45)</td>
<td>52 (34)</td>
</tr>
</tbody>
</table>

Table 2—Results of All Gastric Aspirate and Induced Sputum Cultures in 155 Untreated Tuberculous Patients

<table>
<thead>
<tr>
<th>Cultures Positive (Per Cent)</th>
<th>Cultures Negative (Per Cent)</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Aspirates</td>
<td>59 (30)</td>
<td>135 (70)</td>
</tr>
<tr>
<td>Induced Sputa</td>
<td>176 (51)</td>
<td>168 (49)</td>
</tr>
</tbody>
</table>

RESULTS OF ALL Gastric and Induced Sputum Cultures in 72 Untreated, Bacteriologically Confirmed Tuberculous Patients

<table>
<thead>
<tr>
<th>Cultures Positive (Per Cent)</th>
<th>Cultures Negative (Per Cent)</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Aspirates</td>
<td>53 (38)</td>
<td>87 (62)</td>
</tr>
<tr>
<td>Induced Sputa</td>
<td>176 (69)</td>
<td>78 (31)</td>
</tr>
</tbody>
</table>

p<0.001
In 24 patients with bacteriologically proved tuberculosis, three or more gastric aspirates and three or more aerosol-induced sputum specimens were cultured. Induced sputum specimens were positive on culture in 23 cases (96 per cent) and gastric aspirates in 17 cases (71 per cent), a difference significant at the 0.05 level of probability. In seven instances (29 per cent), induced sputa provided bacteriologic proof of tuberculosis while simultaneous gastric cultures were negative. In only one case (4 per cent) were gastric cultures alone positive (Table 3).

The remaining 70 adults with active tuberculosis who had received chemotherapy prior to admission were evaluated as a separate group in order to assess the effect of such therapy on the likelihood of obtaining positive cultures by any combination of the three techniques (Table 4). Only 60 per cent had positive cultures despite the fact that the proportion of cases in the moderately and far advanced categories was higher than in the untreated group where 79 per cent had positive cultures. The difference is statistically highly significant ($X^2 = 8.5, p<0.005$). Although the percentage of positive cultures was reduced when compared to the untreated group in all categories, this was most striking in the patients with minimal disease, of whom only one of 11 individuals (9 per cent) had a positive culture on admission to the hospital.

**Table 3—Results of Gastric and Induced Sputum Cultures in 24 Patients with Bacteriologically Proven Tuberculosis**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Gastrics Positive</th>
<th>Gastrics Negative</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induced sputa positive</td>
<td>16</td>
<td>7</td>
<td>23 (96%)</td>
</tr>
<tr>
<td>Induced sputa negative</td>
<td>1</td>
<td>0</td>
<td>1 (4%)</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>17 (71%)</strong></td>
<td><strong>7 (29%)</strong></td>
<td><strong>p&lt;0.05</strong></td>
</tr>
</tbody>
</table>

**Comments**

The traditional method for obtaining bacteriologic proof of active pulmonary tuberculosis is the study of specimens of spontaneously produced sputum collected by the patient over a period of 24 hours or more. In patients with a good productive cough, this method approaches the ideal in many ways: it is simple, artrumatic and easily understood by the patient; no equipment is required; close professional supervision is unnecessary; and collection may be accomplished by outpatients.

Because many patients with suspected pulmonary tuberculosis cannot produce sputum even on repeated attempts after careful instruction, other methods are necessary for these individuals. In our experience, the “forced” spuata obtained by exhortation and indoctrination are in reality saliva and of little value. Tracheal lavage demands the services of an experienced physician and elicits an explosive cough hazardous to the operator. Obtaining specimens by laryngeal swabs also requires skilled professional personnel, and these have been found to be inferior to gastric aspirates.**4** Washings obtained at bronchoscopy are not ideal for routine use. Gastric aspirates and, more recently, aerosol-induced sputum specimens have achieved wide acceptance as the most satisfactory accessory procedures to supplement spon-
taneously produced sputum collections in
most institutions.

Cultures of spontaneously produced sputa were adequate for the bacteriologic
proof of pulmonary tuberculosis in 45 per
cent of the untreated patients in the present
study. In patients with a productive cough,
this method was highly efficient, resulting
in positive cultures in 86 per cent. The un-
questionable value of gastric aspirates and
induced sputa in individuals without a pro-
ductive cough is evidenced by the increase
in the incidence of positive cultures to 79
per cent when results obtained by all three
techniques are considered, an increase of
34 per cent over spontaneous sputa alone.

If one accepts, therefore, the demon-
strable diagnostic efficiency of cultures of
spontaneously produced sputa in approxi-
mately half of all cases of pulmonary tu-
berculosis and the value of these two addi-
tional methods in the other half, the ques-
tions to be answered are: (1) is there an
advantage in those patients with nonpro-
ductive cough of gastric aspirates over aero-
sol-induced sputa, or vice versa? (2) do
both techniques supplement each other?

Obtaining gastric aspirates requires a
minimum of equipment, the services of a
nurse or a physician, and a period of vari-
able discomfort and trauma for the patient.
The collection of aerosol-induced sputa nec-
essitates more elaborate, but relatively in-
expensive, equipment which must be
 cleaned and maintained; instruction, al-
though not supervision, by hospital person-
 nel; the use of prepared solutions; and
 minor discomfort for the patient. None of
these limitations is insuperable in even the
smallest hospital or clinic.

Since the introduction by Bickerman,
Sproul, and Barach of the heated hypertonic
aerosol method of inducing sputum produc-
tion, many investigators have demon-
strated the adequacy of bronchial secre-
tions obtained thereby for the diagnosis of
lung cancer. Swartz and Small and Lille-
hei have previously reported the applica-
tion of this method to the study of patients
with suspected tuberculosis. Although their
enthusiastic reports introduced the wide-
spread use of this technique, their study
populations had such heterogenous char-
acteristics that a satisfactory evaluation
from their data of the value of induced
sputa in obtaining positive cultures is not
possible. Beck and Nanda found induced
sputa superior to spontaneous sputa in 11
patients with bacteriologically proved tu-
berculosis. Hensler, Spivey and Dees, rep-
porting a prospective study of 39 tubercu-
losus patients wherein induced sputa and
gastric aspirates were collected concurrent-
ly, noted a greater number of positive cul-
tures with the former technique. Elliott and
Reichel compared the relative efficacy of
gastric aspirates and induced sputa in 105
patients with active tuberculosis. Positive
cultures were obtained in 66 cases (63 per
cent); 44 patients had positive cultures by
both techniques, 16 had positive induced
sputa and negative gastric aspirates and
six had positive gastric aspirates and nega-
tive induced sputa. They concluded that
the two techniques complemented each
other and that both were valuable. Unfor-
nately, 30 of their patients had received
prior antituberculosis chemotherapy, there-
by introducing a variable which, although
as demonstrated in the present report, re-
results in a decrease in the overall yield of
positive cultures, is none the less quite un-
predictable in an individual case or small
series.

The observations of Hensler's group
and of Elliott and Reichel regarding the
proportion of all cultures found to be posi-
tive are comparable to that observed in the
present report. The former authors noted
that 30 per cent of all gastric cultures were
positive as compared to 53 per cent of in-
duced sputum cultures, and the latter
found these figures to be 34 per cent and
47 per cent, respectively. The present study
demonstrates similar findings of 30 per cent
positive gastric and 51 per cent positive
induced sputa. Hence the overall efficiency
of induced sputa over gastric aspirates is
clearly apparent and statistically highly
significant. When results from our bacterio-
logically proved cases of tuberculosis are compared, this discrepancy is even more marked: 38 per cent positive gastric aspirates as compared to 68 per cent positive induced sputa, again a difference which is highly significant.

The superiority of induced sputa over gastric aspirates in individual cases is also statistically demonstrable in the group of 24 untreated individuals with bacteriologically proved tuberculosis who submitted three or more specimens by each technique. Induced sputa were positive on culture in 23 cases (96 per cent) and gastric aspirates in 17 cases (71 per cent). In seven instances (29 per cent) induced sputa provided bacteriologic proof of tuberculosis while simultaneous gastric cultures were negative. In only one case (4 per cent) were gastric cultures alone positive.

Cultures of spontaneously produced sputa remain the most valuable single method of obtaining bacteriologic proof of tuberculosis. In these patients with a good productive cough, diagnostic efficiency is very good. When this technique is supplemented by induced sputa in those patients with poor or absent sputum production, the percentage of cultural confirmation of tuberculosis should approach 80 per cent in patients who have not recently received chemotherapy. Gastric aspirates have a place only in the rare individual (approximately one in 25) who cannot produce sputum even after inhaling the heated hypertonic aerosol. Continued reliance on gastric aspiration ignores a simple, efficient and atraumatic method which is superior in achieving the ultimate goal of all methods for obtaining pulmonary secretions in patients with suspected tuberculosis: cultural proof of active disease. There is little evidence to suggest that both techniques supplement each other and that they are therefore indicated in combination in non-coughing patients.

**Summary**

The relative efficacy of three techniques widely used for collection of pulmonary secretions for bacteriologic study was ascertained in 155 patients with active pulmonary tuberculosis. Tubercle bacilli were recovered by cultures of specimens of spontaneously produced sputum, aerosol-induced sputum or gastric aspirates, all collected prior to chemotherapy, in 122 patients (79 per cent). In 70 patients (45 per cent), the ideally simple technique of spontaneously produced sputum was adequate for bacteriologic diagnosis. Cultures of gastric aspirates and induced sputa greatly increased the yield of positive cultures in the remaining patients, being positive in 52 additional patients (34 per cent).

When results obtained with gastric aspirates were compared to those obtained with induced sputa, the latter technique was significantly superior. In patients without a productive cough, the heated aerosol technique for sputum induction is, with rare exceptions, clearly preferable to gastric aspiration in the bacteriologic diagnosis of pulmonary tuberculosis.

**Resumen**

En 155 pacientes con tuberculosis pulmonar activa se ha determinado la relativa eficacia de tres técnicas generalmente empleadas en la obtención de secreciones pulmonares para el examen bacteriológico. Con este fin se realizaron cultivos de muestras obtenidas por expectoración espontánea, por aspiración del residuo gástrico y mediante aerolización previa. En 122 casos la muestra fue obtenida antes de la instauración de la quimioterapia. En 75 pacientes (45%) el simple empleo de la expectoración espontánea fue suficiente para el diagnóstico bacteriológico. El empleo de la aspiración gástrica y de la expectoración provocada por aerolización aumentó grandemente el rendimiento de cultivos en los sujetos restantes, habiéndose obtenido cultivos positivos en 52 pacientes adicionales (34%).

Cuando se compararon los resultados de las aspiraciones gástricas con los de la aerolización esta última técnica parece ser superior en sujetos sin tos productiva la técnica del aerosol calentado es, con raras excepciones, claramente preferible a la aspiración gástrica en el diagnóstico bacteriológico de la tuberculosis pulmonar.

**Résumé**

La valeur relative de trois techniques largement utilisées pour le recueil des sécrétations pulmonaires afin de les étudier bactériologiquement a été précisée chez 155 malades atteints de Koch ont été recherchés par culture soit des tuberculeuse pulmonaire évolutive. Les bacilles de
Diseases of the Chest

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tuberkulose pnCf#{233}rahle lee positives fit kulose.

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und material Die Chez l'examen malades positives a Magenspiilfluissigkeit von zwar assurer durch produktem dtir durch at, durch die produziertem durch Kulturagensus, durch die produziertem durch a Vom Magenspiilfliis- Magenspiilfliis- von 122 Patienten (79%) ergab bei 70 Patienten (45%), da die ideale einfache Technik von spontan produziertem Sputum fur die bakteriologische Diagnose adquat war. Kulturen von Magenspiilfliissigkeit und knstlich erzeugtem Sputum erhhten ganz wesentlich die Ausbeute an positiven Kulturen bei den iibrigen Patienten, und zwar ergaben sich positive Werte bei 52 weiteren Fllen (34%).

wurden die Resultate, die mit Magenspiilfliissigkeit gewonnen waren verglichen mit denjenigen, die mit Inhalation gewonnenen Sputum erzielt worden waren, so war die letzterwnte Technik signifikant gnstiger Bei solchen ohne produktiven Husten ist die Aerosoltechnik zur Sputumgewinnung mit trwarnten Aerosol, von seltenen Ausnahmen abgesehen, eindeutig der Magenspiilfliissigkeitgewinnung vorzuziehen bei der bakteriologischen Diagnose der Lungentuberkulose.

ZUSAMMENFASSUNG

Die relative Ergiebigkeit der drei in groen Umfang benutzten Techniken zur Gewinnung von Lungensekret f黵 bakteriologische Untersuchungen wurde in 155 Fllen mit aktiver Lungentuberkulose berprft. Tuberkelbazillen wurden ermittelt durch Kulturen von Paraparen von spontan produziertem Sputum, durch Aerosol gewonnenen Sputum oder durch Magenspuiflissigkeit. Von der Chemotherapie gesammeltes Material von 122 Patienten (79%) ergab bei 70 Patienten (45%), da die ideale einfache Technik von spontan produziertem Sputum f黵 die bakteriologische Diagnose adquat war. Kulturen von Magenspuiflissigkeit und knstlich erzeugtem Sputum erhhten ganz wesentlich die Ausbeute an positiven Kulturen bei den iibrigen Patienten, und zwar ergaben sich positive Werte bei 52 weiteren Fllen (34%).

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3 Handbook of Tuberculosis Laboratory Methods, Veterans Administration—Armed Forces Cooperative Study on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C., 1962.

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