Lesions of Swine Lymph Nodes as a Diagnostic Test to Determine Mycobacterial Infection

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Decisions as to the disposition of swine carcasses with lesions attributable to a mycobacterial infection are based upon a lesion criterion which is used as a diagnostic test by federal meat inspectors. Using this criterion, a federal meat inspector classified 58 of 100 pigs as “passed for cooking” and the other 42 pigs passed. Of the 58 pigs passed for cooking and the 42 pigs passed, mycobacterial isolations were made from the lymph nodes of 33 and 15 of the animals, respectively. The lesion criterion as a diagnostic test has the following attributes: 70% sensitive; 53% specific; 23% index of performance; 57% positive accuracy; and 67% negative accuracy.

Swine mycobacteriosis, erroneously described as swine “tuberculosis,” is diagnosed presumptively in slaughter houses by meat inspectors when they detect mycobacteria-like lesions in carcasses. The gross pathology of these lesions varies from pinpoint-size caseous nodules to pea-size caseo-calcareous nodules (6). The smaller-size lesions predominate and characteristically are few in number, usually located in the cervical and mesenteric lymph nodes. When mycobacteria are isolated from these lesions they are invariably of the Mycobacterium avium-intracellulare complex (8).

The Federal Meat and Poultry Inspection regulations concerned with swine tuberculosis are based upon considering mycobacteria-like lesions as pathogenic for mycobacterial infection and the establishment of a gradation of infection which decided the disposition of a swine carcass (1). Briefly, these regulations are: (i) carcasses with lesions in one organ system (usually the cervical lymph nodes) are passed for human consumption after removal of the affected part; (ii) carcasses with lesions in two organ systems (usually the cervical and mesenteric lymph nodes) are “passed for cooking,” which means the carcass must be cooked at 77°C for 30 min before entering the food chain; (iii) carcasses with lesions that involve organs like the liver are considered to have a generalized infection and are condemned.

The disposition criteria are based upon recommendations set forth in a report to the U.S. Department of Agriculture by a Special Committee of the Department of Health, Education and Welfare (DHEW) in 1970 and reaffirmed in 1976 (11). The basis for the recommendations is that in the absence of evidence to the contrary, mycobacterial infections of swine must be considered a potential human health hazard. To minimize this hazard, the intent of the recommendations was to prevent handling and/or consumption of mycobacterially infected tissues because no evidence existed that eating uncooked or undercooked meat containing mammalian mycobacteria would not result in infection in humans. Of the approximately 75,000,000 swine slaughtered annually, about 50,000 are considered tubercular and unfit for human consumption unless cooked (10).

Echoing the concerns of the 1970 Special Committee of DHEW, the 1976 Committee concluded that it was difficult to define which tissues were and which tissues were not “infected” and what is “localized” or “generalized.” For these reasons, the 1976 Committee strongly urged that these and other pertinent issues of swine mycobacteriosis be resolved.

It has been recognized for about 40 to 50 years that the lesion criterion could only provide the basis for a presumptive diagnosis of mycobacterial infection. A high percentage of isolation attempts from lymph nodes with mycobacteri-like lesions failed to yield mycobacteria (5). These failures may have been due to: (i) inadequacy of isolation method; (ii) the process had healed and no living bacilli were present; (iii) the lesions were caused by organisms other than mycobacteria. On the other hand, mycobacteria have been isolated from normal-appearing lymph nodes of swine (4). The lymph nodes appeared normal because M. avium-intracellu-
ine infections in swine show little tendency to caseate (4).

Several investigators have established that localized lesions occasionally reflect generalized infection in that tubercle bacilli could be recovered from normal-appearing tissues such as muscle, intramuscular lymph nodes, heart blood, uterus, spleen, and livers of cattle, calves, and swine (4). Feldman established that M. avium could be isolated from intramuscular lymph nodes of swine not immediately adjacent to a demonstrable lesion; this suggested the possibility of an occasional dissemination of mycobacteria in the blood stream (3).

Diagnostic tests are usually evaluated by testing a population of subjects known to be positive or negative for the condition the test is designed to detect (2). If this evaluation is successful, further evaluations are conducted in populations whose condition is unknown. In this manner, the predictive accuracy of a diagnostic test can be established.

In one study, mycobacteria were isolated from 79% of the 2,036 swine lymph node samples with lesions attributable to a mycobacterial infection (8). Citing this work, and a second study in which histopathological examination and mycobacterial isolation demonstrated that 91% of suspected swine lymph nodes contained mycobacteria, it was stated that mycobacterial diagnosis based on gross appearance of lesions is "highly commendable" [G. B. Snyder, Symposium on Swine Mycobacterial (T.B.) Infections, Madison, Wis., 1975]. In these studies, the only lymph nodes examined were those with lesions attributable to a mycobacterial infection. Therefore, the lesion criterion as a diagnostic test for mycobacterial infection has never been established.

The minimum requirement for a test to qualify as a test for a disease is that it detects disease better than chance alone (7). If this minimal requirement does not seem high enough to justify using a test under certain circumstances, then a higher standard can be required. In this study, an 80% agreement between the results of the lesion criterion and mycobacterial isolation was set as the standard.

MATERIALS AND METHODS

In a period of 3 months a federal meat inspector chose different swine herds to collect lymph node samples from 58 swine passed for cooking (lesions in two organ systems each attributable to a mycobacterial infection) and 42 swine passed for human consumption (no lesions). The rationale for selecting this population, for this study, was to ensure that the mycobacterial background prevalence would be high (7). The sample from the swine passed for cooking was one cervical and one mesenteric lymph node with lesions. The sample from the swine passed was one cervical and one mesenteric lymph node selected haphazardly. The samples from each pig were pooled, coded to avoid bias, and routinely processed for mycobacterial isolation (9).

As described previously, the preferred method of evaluating a diagnostic test is to perform the test on subjects known to be positive or negative for the condition in question. An alternative method for evaluating a diagnostic test is to group the subjects according to the test results and then to determine the actual condition of the subjects (2). In this instance, the lesion criterion was used to group swine either positive or negative for mycobacteria-like lesions, and mycobacterial isolation was used to determine the actual condition (2). Calculations were then made for prevalence rate, sensitivity, specificity, index of performance (with standard error), and the predictive accuracy of the test (2, 7, 12). These terms are defined as follows: prevalence—the proportion of swine with mycobacterial infections; sensitivity—the chance that the test will be positive when applied to swine which have a mycobacterial infection; specificity—the chance that the test will be negative when applied to swine which do not have mycobacterial infection; index of performance—a summary index which combines sensitivity and specificity into a single value; predictive accuracy—how often the test will be correct when the results are either positive or negative. The advantages of the characteristics of sensitivity, specificity, index of performance, and predictive accuracy is that they are independent of the prevalence rate. The determination if there was 80% agreement between the results of the lesion criterion test and mycobacterial isolation was done by utilizing the normal approximation test (z test).

RESULTS

Of the 58 swine passed for cooking and the 42 pigs passed for human consumption, mycobacterial isolations were made from the lymph nodes of 33 and 14, respectively (Table 1). The organisms isolated were M. avium-intracellulare (97.9%) and M. gastri (2.1%).

The prevalence of mycobacterial infection in these swine was 47% (Table 1). The sensitivity (70%) and specificity (53%) of the lesion criterion as a diagnostic test to detect mycobacterial infections are summed by the index of performance of the test, which is 23 ± 19%. The lesion criterion as a diagnostic test meets the minimal requirements of a test in that mycobacteria are isolated from swine designated as positive by the test in more than half of the cases (predictive positive accuracy = 57%) and are not isolated from swine designated as negative by the test in more than half of the cases (predictive negative accuracy = 67%).

Evaluation of the lesion criterion test as being in 80% agreement with mycobacterial isolation demonstrated that neither the positive lesion
TABLE 1. Calculations of prevalence, sensitivity, specificity, index of performance, and the predictive accuracy of the lesion criterion when mycobacterial isolation designates the true condition

<table>
<thead>
<tr>
<th>Swine classificationa</th>
<th>Total</th>
<th>Mycobacteriaa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Isolated</td>
</tr>
<tr>
<td>Passed for cooking</td>
<td>58</td>
<td>33</td>
</tr>
<tr>
<td>Passed</td>
<td>42</td>
<td>14</td>
</tr>
</tbody>
</table>

Sensitivity = 33/47 = 0.70
Specificity = 28/53 = 0.53
Population prevalence = 47/100 = 0.47
Index of performance = 0.70 ± 0.53 – 1 = 0.23
SE\(^c\) of index

\[ SE = \sqrt{(33)/(33 + 14) + (14)/(28 + 14)} \]

\[ = 0.099 \]

95% confidence interval of index of performance = 0.23 ± 0.194
Lower limit = 0.0036; upper limit = 0.424

Predictive accuracy
Positive = 33/58 = 0.57
Negative = 28/42 = 0.67

\(a\) See text for classification.
\(b\) M. avium-intracellulare (97.9%) and M. gastri (2.1%).
\(c\) SE, Standard error.

criterion nor the negative lesion criterion met this standard \((P < 0.001\) and \(P < 0.03\), respectively [Table 2]).

DISCUSSION
The sensitivity (70%), specificity (53%), and 23 ± 19% index of performance indicate that the lesion criterion for declaring swine either positive or negative for mycobacterial infections is a diagnostic test of low caliber. However, the lesion criterion does meet the minimal requirement for being considered a test in that its predictive accuracy (positive = 57%, negative = 67%) is better than 50% (Table 1).

The flaw in this minimal standard for the detection of swine mycobacteriosis is that the estimated prevalence of mycobacterial infection in swine declared negative (14 mycobacterial culture positive/42 swine without lesions) is 33% (Table 1). Therefore, the minimal requirement of a test being better than 50% accurate would always be acceptable in a population with an estimated prevalence of 33%.

To demonstrate the inadequacy of the minimal standard it was hypothesized that there should be 80% agreement with mycobacterial isolation for the positive and negative lesion criteria. In each case, both criteria failed, significantly \((P < 0.001)\) and \((P < 0.03)\), to meet the 80% standard of agreement (Table 2). In the case of the swine positive by the lesion criterion, this has no effect on the possible exposure of the public to living mycobacterial organisms. On the other hand, the failure of the negative aspect of the lesion criterion to eliminate a large percentage of swine which do have mycobacterial infections severely compromises the policy to minimize potential human exposure to living mammalian mycobacteria.

The prevalence rate of 47% for mycobacterial infection, in this study, is undoubtedly understated since only two lymph nodes per swine were bacteriologically cultured for mycobacteria. With a high prevalence of a disease, a test with a high rate of sensitivity will have a high rate of positive accuracy. This situation permitted the conclusion that since mycobacteria were isolated in high percentages from swine with lesions, the test was effective [8; Snyder, Symposium on Swine Mycobacterial (T.B.) Infections, 1975].

Present policy for the disposition of swine carcasses is based upon the lesion criterion as a diagnostic test and the concept of localized lesions. Since M. avium-intracellulare infections

TABLE 2. Evaluating\(^a\) the lesion criterion test with mycobacteria culture against a hypothetical standard of 80% agreement

<table>
<thead>
<tr>
<th>Lesion criterion test</th>
<th>Mycobacteria isolated</th>
<th>Agreement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Positive(^b)</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Negative(^c)</td>
<td>14</td>
<td>28</td>
</tr>
</tbody>
</table>

\(a\) Normal approximation test \((z\) test).
\(b\) Positive criterion:
\[ z = 0.569 - 0.80 / \sqrt{(0.80)(0.20)/58} = 4.4 \ (P < 0.001) \]

95% confidence limit of percent agreement:
0.569 ± 1.96 \((0.569)(0.431)/58\)
0.569 ± 0.127
lower limit = 0.442; upper limit = 0.696

\(c\) Negative criterion:
\[ z = 0.667 - 0.80 / \sqrt{(0.80)(0.20)/42} = 2.15 \ (P < 0.03) \]

95% confidence limit of percent agreement:
0.667 ± 1.96 \((0.667)(0.333)/42\)
0.667 ± 0.143
lower limit = 0.524; upper limit = 0.81

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of swine show little tendency to caseate, these organisms have been isolated from major organs of swine which appear normal (4). If a swine carcass had lesions attributable to a mycobacterial infection in these organs, the carcass would be considered unfit for human consumption and condemned. Therefore, the concerns of the 1976 Special Committee of the DHEW, described previously, appear to be well founded in that it has been suggested that localized lesions might reflect generalized disease since mycobacteria may be occasionally disseminated in the blood stream from localized lesions (3, 4).

In swine, the absence of lesions attributable to a mycobacterial infection does not mean the absence of either a localized or a generalized infection. Therefore, the number of swine carcasses with mycobacterial infection passed for human consumption is that proportion of the infected swine population (in this study, 33%) which does not have lesions attributable to a mycobacterial infection. This suggests that the use of the lesion criterion to diagnose mycobacterial infection in swine needs to be augmented by the addition of another diagnostic test such as the tuberculin test.

LITERATURE CITED