

COCCIDIOIDOMYCOSIS COOPERATIVE STUDY

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AGENDA

Meetings held at the Veterans Administration Regional Office, Los Angeles, California.

Laboratory Committee -- Nov. 29, 1956 -- Chairman, M. Huppert, Ph.D.

1. Objectives and background data
2. Detailed review of laboratory phases of the Report Form
3. Laboratory diagnostic standards - cultural, serological, pathological, and animal pathogenicity
4. Minimum safety requirements in a laboratory handling C. immitis
5. Establishment of a C. immitis culture bank at the San Fernando VAH
6. Future research plans and protocols

Committee on Plans -- Nov. 30, 1956 -- Chairman, D. Salkin, M.D.

1. Review of clinical aspects of the disease
2. Detailed review of the Report Form
3. Discussion of specific items
4. Business and administration

In Attendance

Laboratory Committee -- Drs. Huppert (Ch.), Armstrong, Brosbe, Ende, Hall, Miss Campbell. Absent: C. E. Smith
Committee on Plans ---- Drs. Salkin (Ch.), Hensler, Hood (for Dr. Canada), Hyde, Netzer, Ringle, Steele, Wier, Huppert (Lab. Comm.). Absent: Egeberg
Central Office ----- Drs. Chapple, Dunner, Holt, Mrs. Livings
Guests ----- Drs. Kurnick, Myers
Recording Secretary --- Dr. L. G. Wayne

PROCEEDINGS OF THE COMMITTEE ON PLANS

1. Review of the clinical aspects of the disease

- (1) Epidemiology - endemic areas, occupational hazards, incidence of infection in various areas among residents; communicability
- (2) Pathology - primary infection, residuals, dissemination into other organs especially bones, viscera, brain, skin
- (3) Clinical picture -
 - Primary - subclinical, clinical
 - Dissemination - racial factors, prognosis, longevity
 - Residuals - cavity, solid foci, calcification
- (4) Behaviour of residual cavities - asymptomatic states
- (5) Coccidioidomycosis and Tuberculosis
- (6) Skin test, precipitins, complement fixation
- (7) Roentgenology - findings in primary and residual coccidioidomycosis; disseminated foci; correlation of roentgen and clinical findings
- (8) Mycological studies
- (9) Diagnostic criteria - history of exposure, clinical picture, physical examination, X-ray, mycology and serology, biopsy, skin test
- (10) Treatment
 - Rest - use of serology as a guide
 - Specifics - none
 - Supportive measures
 - Corticosteroids
 - Surgery - indications and contraindications
 - collapse measures, resection
 - bone and joint and other areas

2. Report Form - Data used from above to draw up the Report Form

Every item reviewed and discussed in detail. The main sections include identification data, clinical aspects, laboratory data, therapy, surgical therapy, resection mycology, resection pathology, autopsy data. The immediate objectives of this retrospective study are: (1) to determine the number and types of cases available for future studies; (2) to test the mechanics of the cooperative study; (3) to serve as the first step in establishing a Case Registry.

3. Specific Topics Discussed

- (1) Skin test - to use a standard batch of antigen, to specify source, and dilution; intracutaneous to be read similar to a tuberculin test at 48 hours in mm. of the indurated area. There was much argument whether to record it in mm. or in 1 to 4 plus as for a tuberculin; the majority voted for the former. To use the flexor surface of the forearm.
- (2) Bronchograms in cavitary cases - discussed and decided to do only when clinical and roentgen indications demand it.
- (3) Classification and terminology - such as primary infection, residual disease, activity and inactivity should be reviewed at some later date.

- (4) Retrospective data to be gathered by the Report Form - on patients admitted to the hospital between January 1, 1955 and January 1, 1957. To include all hospitalized veterans and armed forces personnel but to exclude their dependents. The study may go further back depending upon the data obtained.
- (5) Future Protocol studies to be considered:
 - (a) Use of fungicides when made available
 - (b) Surgical resection of residual cavities
 - (c) Surgical resection of residual non-cavernous foci
 - (d) Use of bed rest and limited activity in treatment of acute and subacute infections
 - (e) Use of corticosteroids
 - (f) Use of palliative and supportive measures
- (6) Future material available - The importance of this disease will undoubtedly increase because of the tremendous immigration of peoples into the coccidioidomycosis endemic areas (some estimates indicate one-half million per year), the numbers who travel through the endemic areas, and the numbers of Armed Forces personnel serving in these areas. It is estimated that 90 per cent of those residing in endemic areas develop positive skin tests within 10 years.

4. Business and Administration

- (1) A report of this meeting to be given by Dr. John Steele to the Veterans Administration Research Conference at Memphis, December 11, 1956.
- (2) Meeting at St. Louis during the Chemotherapy Conference, Tuesday, February 12, 1957, to inform other study units of the status of the program
- (3) Probable small informal meeting at Pleasanton, California, March 12, 1957.
- (4) The Quarterly Reports may be used by individual hospitals for various reports on coccidioidomycosis and announcements (Dunner)
- (5) To encourage distribution of Dr. Egeberg's film on coccidioidomycosis
- (6) Study Units to include: Army; Navy; Air Force; VA Hospitals Long Beach, San Fernando, Fresno, Livermore, Albuquerque, Whipple, Tucson, Phoenix, Houston, Dallas, McKinney, Temple, Kerrville and others interested
- (7) For this retrospective study, the hospitals to be included will be those in the endemic areas. This will be only for the first trial test of the Report Forms; later study will include all the VA-Armed Forces Units. It was suggested that, in the endemic area hospitals, one physician should be designated to complete the Form. For the other hospitals, the data will be called in by Central Office and sent to Dr. Hyde who graciously volunteered to complete the Form. The Armed Forces representatives discussed the possibility of one unit being responsible for the Forms and even a future consolidation of active cases in one study hospital for each branch of the service, after a preliminary trial of the Form.
- (8) It is planned to issue a bulletin containing tentative clinical and laboratory standards drawn up by authoritative workers in this field (similar to National Tuberculosis Association booklet on Diagnostic Standards).

PROCEEDINGS OF THE LABORATORY COMMITTEE

1. Objectives and background data

Dr. Salkin briefly reviewed the recommendations made at the two previous preliminary meetings and outlined the objectives of the present program. He indicated that the most pressing problems were the ultimate fate of the sub-acute and chronic cases, therapy, and the establishment of a laboratory program covering minimum standards for microbiological and serological diagnosis, and for testing potential chemotherapeutic agents in anticipation of their becoming available in increasing variety. Dr. Salkin pointed out that the principal recommendation of the preliminary meetings was that a report form should be composed to collect pertinent information from past records to serve as a foundation for future protocol studies.

2. Report Form

A proposed Report Form for the Coccidioidomycosis Cooperative Study had been circulated to the members of both committees and it was submitted for discussion of the laboratory phases of the form. Certain changes were suggested and approved by the committee. These changes have been incorporated into the revised form which is appended. It was agreed that Mrs. Livings would be free to select the final format, and that the information requested should be extended to include disseminated disease and autopsy findings.

3. Minimum standards for laboratory diagnosis

The members of the committee agreed that it was desirable to set minimum requirements for a laboratory diagnosis of coccidioidomycosis. The points discussed included the collection of the specimen, culturing the specimen, the handling and identification of the culture, the demonstration of pathogenicity for experimental animals, and the patient's serology. It was pointed out that a uniform and plentiful source of antigen should be available for all stations cooperating in any future protocol involving serology or skin testing. The suggestion was made that a request be submitted to Dr. C. E. Smith for the assignment of a complete lot of antigen for the exclusive use of the units participating in such a program. The complete recommendations of the committee are appended. It was suggested that these recommendations be given the widest dissemination possible.

4. Minimum safety requirements

The committee discussed the dangers in handling cultures of C. immitis. All members agreed that transfers of such cultures should be made in a bacteriological hood. Dr. Holt felt strongly about this point and expressed his opinion that transfers outside of a bacteriological hood should be forbidden. Dr. Huppert suggested the use of a prescription bottle fitted with a screw-cap containing a rubber diaphragm. After a culture had grown in a bottle, fluid could be injected to make a suspension which could be withdrawn to be used either for transfer or for inoculating experimental animals. The culture could be killed by injecting formalin before opening the bottle to make preparations for microscopic observation. With this technique a viable culture need not be opened at any time. Dr. Huppert expressed his opinion that even with this method all C. immitis cultures should be handled

in a bacteriological hood for added safety. The committee recommended that cultures of this fungus should be manipulated only within a bacteriological hood. It was recommended also that personnel working with C. immitis cultures wear face masks at least, and that personnel handling infected animals wear surgical gloves. Personnel should be skin tested every three months if negative and have an X-ray every six months.

5. Culture bank

The committee recommended that it would be most desirable to establish a culture bank as a source of reference cultures for use in future investigations. The facilities of the Mycology Research Laboratory, San Fernando VAH, were offered for this purpose. It was noted that a culture bank program had been initiated already at this station and that transfers of all strains of C. immitis were desired. The committee recommended that cultures could be prepared for shipment to this station in either of two ways: 1/ grown cultures should be covered with sterile mineral oil; 2/ cultures could be shipped immediately after inoculation to fresh media and before having an opportunity to grow. These cultures should be in heavy-walled screw-cap bottles or tubes, packed in cotton in a double mailing carton, and shipped by Registered Mail. Dr. Steele suggested that Dr. Steenken be asked for pointers on running a culture bank.

6. Future research plans

Very little time remained for a discussion of research protocols. It was suggested that such programs be continued on an individual station basis, and that future protocols on a cooperative level might develop from information obtained via the Report Form. It was to be anticipated that such studies would deal with the biology and immunology of C. immitis, and with testing potential chemotherapeutic agents. For these, a culture bank was a virtual necessity and a start had been made in this direction. Miss Campbell suggested that the gastro-intestinal tract might be a fruitful source of inhibitory agents since C. immitis does not invade this site.