# Technical Papers

## The Infectiousness of Coccidioidomycosis

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Coccidioidomycosis is an infectious disease caused by the fungus, *Coccidioides immitis*. The respiratory tract is the usual portal of entry. The fungus causes either a benign, self-limiting disease of the lung or a progressive, chronic and malignant process which may spread from the lung to localize in any or all organs of the body. The disease is endemic in San Joaquin Valley, California, as well as in parts of Texas, Arizona, and New Mexico. With the training of troops in these states, and their subsequent demobilization, numerous soldiers harboring the fungus will return to all parts of the United States.

It is universally reported that the disease is not contagious, there being no direct man-to-man or animal-to-man spread, and that there is therefore no reason for elaborate isolation (*1–4*). The general consensus of opinion is that the spherule or endospore-filled sporangium stage of the fungus found in animal tissue goes through a stage of development in nature to produce mycelial threads and spores (chlamydospores), when it becomes infective by the respiratory route for humans and animals. Rodents have been considered the reservoir for the disease (*1*).

The following experiments demonstrate that it is possible to transmit the disease, by bronchial installation of spherules, from man to animal and from animal to animal. These findings must alter our stand regarding the isolation of diseased patients.

The method employed was to instill spherule-containing exudates into the bronchi of guinea pigs (by means of a catheter or blunt needle) and to propel the exudate into the smaller bronchi ramifications and alveoli by applying a minimal amount of air pressure. This method was used by the senior author to produce lung abscesses in dogs and was later modified by Robertson to produce lobar pneumonia.

Sixteen guinea pigs were thus injected, using exudate from a sacroiliac abscess, a psoas abscess, and an emulsion of hilus lymph nodes from a human case and from a neck abscess of a guinea pig. The animals (14) were sacrificed at various intervals from 8 to 63 days (two died at 18 and 28 days). Infection localized to the lung occurred in every case varying from a typical primary complex of the lung, where a single lesion was noted in one lobe, and a corresponding enlarged hilus lymph node, to the involvement of all lobes simulating lobar pneumonia. Generalization did not occur in any case.

Microscopically, typical granulomata containing spherules in every stage of development were noted in the lung and draining lymph nodes. Direct NaOH mounts and/or cultures of lungs and nodes were positive for *C. immitis* in practically every instance.

The gross and microscopic lesions (especially the single localized lesions in the lung) more closely resemble the human infections than those produced in animals by the inhalation of chlamydospores.

These experiments show that the spherules direct from human or animal sources are infective through the respiratory tract. Thus, all active human cases of primary or secondary coccidioidomycosis should be considered contagious until proven otherwise.

### References

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## Effect of Rubber Tubing Upon the Stability of Penicillin and Streptomycin Solutions

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S. L. Cowan (*1*) has reported the inactivating effect of synthetic rubber upon solutions of penicillin. Since no work upon this important problem has been reported in the United States, we have investigated the suitability of a variety of rubbers for the parenteral administration of penicillin and streptomycin.

Solutions of penicillin and of streptomycin were placed in separate sterile three-foot lengths of the various samples of rubber tubing. For controls, the solutions were also placed in glass tubing. At the end of 6 and 24 hours samples were withdrawn for assay.

The solutions of streptomycin were assayed by the filter-paper disc method with *Bacillus subtilis* as the test organism. The penicillin solutions were assayed according to directions given in "A tentative penicil-

[1] We wish to express our gratitude to the B. F. Goodrich Company, Harshaw Chemical Company, Fisher Scientific Company, and Chemical Rubber Company for samples of rubber used in this investigation.

lin-sodium monograph" (Washington Conference, 17 February 1944).

The effects of the various rubber samples upon the stability of penicillin and streptomycin solutions are shown in Tables 1 and 2, respectively.

TABLE 1

EFFECT OF SYNTHETIC AND NATURAL RUBBERS UPON THE STABILITY OF PENICILLIN SOLUTIONS*

| Description | Type | Unitage at end of 6 hr. | Unitage at end of 24 hr. |
|---|---|---|---|
| White surgical Koroseal | Synthetic | 70 | 36 |
| GN black | " | 95 | 16 |
| Black Koroseal | " | 97 | 73 |
| S black | " | 111 | 86 |
| Buna | " | 82 | 0 |
| Buna white | " | 121 | 114 |
| White plastic | " | 111 | 93 |
| Neoprene black | " | 74 | 0 |
| Pure gum black | Natural | 96 | 0 |
| GRS black | Synthetic | 79 | 0 |
| Buna S | " | 50 | 0 |
| Tygon | " | 91 | 85 |
| Amber latex | Natural | 87 | 94 |
| Crepe rubber | " | 105 | 99 |
| Natural rubber | " | 117 | 93 |
| Anode amber | " | 105 | 93 |
| Glass tubing | ..... | 108 | 106 |

* The solution was made up to contain 100 units/ml.

TABLE 2

EFFECT OF SYNTHETIC AND NATURAL RUBBERS UPON THE STABILITY OF STREPTOMYCIN SOLUTIONS*

| Description | Type | μg./ml. at end of 6 hr. | μg./ml. at end of 24 hr. |
|---|---|---|---|
| White surgical Koroseal | Synthetic | 37 | 43 |
| GN black | " | 40 | 49 |
| Black Koroseal | " | 40 | 50 |
| S black | " | 40 | 39 |
| Buna | " | 43 | 50 |
| Buna white | " | 46 | 39 |
| White plastic | " | 43 | 40 |
| Neoprene black | " | 43 | 34 |
| Pure gum black | Natural | 40 | 44 |
| GRS black | Synthetic | 34 | 44 |
| Buna S | " | 46 | 43 |
| Tygon | " | 43 | 50 |
| Amber latex | Natural | 46 | 34 |
| Crepe rubber | " | 43 | 34 |
| Natural rubber | " | 40 | 56 |
| Anode amber | " | 40 | 54 |
| Glass tubing | ..... | 34 | 42 |

* The solution was made up to contain 50 μg./ml.

Of 11 samples of synthetic rubber tested, 4 inactivated penicillin completely in 24 hours. Two other samples caused 64 and 84 per cent reductions in the activity of the penicillin during the same period. Of 5 samples of natural rubber tested, 1 pigmented sample inactivated penicillin completely in 24 hours.

Buna S rubber caused a 50 per cent reduction of penicillin activity in 6 hours. Other samples of synthetic rubber reduced the activity of penicillin 20–30 per cent in the same period.

None of the samples of rubber tubing tested caused any reduction in the activity of streptomycin.

This study is not intended as a complete investigation of the effects of rubber upon antibiotics. It is evident, however, that for continuous drip procedures some attention must be given to the type of rubber used for the administration of penicillin. It is of interest to note that white surgical Koroseal caused a drastic reduction in penicillin activity, while black synthetic Koroseal caused only a moderate inactivation of the antibiotic.

It is suggested that rubber tubing intended for hospital usage be checked for inactivating effects upon antibiotics and that acceptable tubing be appropriately designated.

### Reference

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## Comparative Toxicity of DDT and Four Analogues to Goldfish, Gambusia, and Culex Larvae

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The large-scale use of DDT in natural areas makes it necessary to study the effects it and related compounds have on all forms of life if control measures are to be developed.

Of beneficial vertebrate groups, fish have already been shown to be very vulnerable to DDT in the laboratory (*2, 3*). Under natural conditions mortality of fish has been observed where large amounts or repeated doses of DDT were used in the control of mosquito larvae (*7*). We have attempted to determine more accurately the comparative tolerance of fish (goldfish and *Gambusia affinis*) and mosquitoes (*Culex apicalis*) to DDT and especially its p-halogen analogues.

*Procedures.* In addition to the regular DDT or 1-trichloro-2,2-bis(p-chlorophenyl)-ethane (*1*), four analogues were also tested as follows: (1) 1-trichloro-2,2-bis(phenyl)-ethane, which we shall designate as DPT; (2) 1-trichloro-2,2-bis(p-fluorophenyl)-ethane, DFDT; (3) 1-trichloro-2,2-bis(p-bromophenyl)-ethane, DBrDT; and (4) 1-trichloro-2,2-bis(p-iodophenyl)-ethane, DIDT.[1] Summerford synthesized these compounds by condensing benzene or the appropriate halobenzene and chloral with the aid of chlorosulfonic acid, according to a previously described method (*6*).

All tests were run in individual fish bowls containing tap water previously conditioned and oxygenated in a large aquarium containing aquatic plants. One fish and 4 to 10 Culex larvae were placed in each bowl. One ml. of an acetone solution of DDT and its analogues, ranging from 0.0005 to 10 ppm, was added to

[1] The preparation of the p-fluoro and the p-iodo analogues will be described in a subsequent paper, since we have found no published reference to the synthesis of the former compound.