can be arrived at by making a number of oxygen determinations with samples of gas from the inhalation tubing.

There is one outstanding lack of precision in anæsthesia which still cries for an adequate solution. The respiratory minute-volume is not always, but is usually, decreased below normal and this is certainly always true in the deeper anæsthesia required for abdominal relaxation. In proportion to this decrease the patient fails to eliminate carbon dioxide from his blood and the carbon dioxide tension rises. He does not respond to this with increased respiration because his respiratory controls are depressed by the anæsthesia. This upsets the blood pH, mobilizes bases and starts a train of events which interferes with uneventful convalescence. We never know the extent of carbon dioxide retention. We can and do generally obviate it by controlling the respiration through manipulation of the bag, but we can not know whether we are over- or under-ventilating. We greatly need a gadget which will sample the exhaled gas and determine its carbon dioxide tension within a minute. Accordingly we will be able to increase or decrease the respiratory exchange artificially, thus keeping the carbon dioxide tension in the exhaled gas, and so also in the blood, at the normal level. Not until we can accomplish this will we administer truly physiological anæsthesia and return the patient to his bed in the best possible condition.

I believe that a practical instrument for carbon dioxide and respiratory volume control is within reach.

If the respiratory exchange is made adequate to keep the blood carbon dioxide at the normal level, and if at the same time the oxygen in the inspired atmosphere is normal and blood pressure and blood replacement is kept up, one can rest assured that no tissue will suffer from oxygen deficit.

Is it too much to hope that we will some day be equipped for a running electrocardiogram on each anæsthetized patient? We know of an occasibnal death on the table which seems unexplainable. Will we not be justified in adding even this expense to the cost of anæsthesia in order to get possible warning and help for such an occasional patient? Is this too much to add to our standard of living, or prevention of dying?

All the measures of precision mentioned above involve a considerable effort and might be classified by some as nuisances and unwarranted expenses. Few of them are followed with anything like routine in many places. How much of such effort should we put in when the average patient does well without them? The remark may be made, that the skillful anæsthetist does not need such things, he can do as well with the "art of anæsthesia" and, in fact, some may say that such gadgets may be just an effort to turn anæsthesia over to technicians.

I believe that the more skillful and understanding the professional anæsthetist becomes the more he feels the need of more precision methods and the benefits to himself and to his patients to be derived from more precisely controlled physiology. Most advances in anæsthesiology will be along these lines.

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TULARÆMIA*

(With a Report of Nine Cases)

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TULARÆMIA holds a somewhat unique place among human maladies. The causative micro-organism was identified before the disease was recognized in man. Within the 34 years that have elapsed since the first description of the etiological agent we have been furnished with a fairly complete picture of the etiology, epidemiology, pathology and symptomatology of the disease. Further, within the past few months a therapeutic agent has been used which promises to be an effective method of treatment.

Tularæmia gets its name from the fact that the causative micro-organism, *Bacterium tularense*, was discovered by McCoy and Chapin[1] in 1912 as the agent which produced a plague-like disease of ground squirrels in Tulare County, California. The micro-organism was first isolated from man by Wherry and Lamb[2]

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in 1914. Actually tularæmia existed as a human disease for many years prior to this. We owe to Francis[3] the classical description of the natural history of the disease in man.

Tularæmia is widely distributed in the temperate zones, particularly in North America. It is a common disease in Alberta and has been frequently recognized in the rural population since it was first recognized by Shaw and Jamieson[4] in 1931.

The *Bacterium tularense* is a small Gram negative organism which requires special laboratory culture media for growth. Guinea pig inoculation of infected human material is necessary in most cases, to identify the organism.

Epidemiology.—How is the disease contracted in man? The most common reservoir of the disease on this continent is the wild rabbit. Tularæmia exists as a natural infection in rabbits and accounts partly for the periodic increased mortality in this species. The human individual contracts the disease in most cases from the handling of wild rabbits. Most of the cases of disease we have studied have occurred in fur farmers who have skinned rabbits as food for fur-bearing animals. Ground squirrels, wild rats and field mice may also harbor the disease. Tularæmia may be contracted by a bite of a wood tick or a horse fly which has fed on infected animals. Rarer methods of infection are the ingestion of infected rabbit meat or the drinking of water which has been contaminated by infected rats.

Pathology.—Ulceration at the site of infection is followed by enlargement and necrosis of the regional lymph nodes. The infective process may be arrested at this stage or may go on to widespread dissemination of the disease with septicæmia, giving rise to areas of focal necrosis in the spleen, liver and lungs.

Symptoms and signs.—Following an incubation period of one to ten days there is a sudden onset with malaise, chills, fever and headache. The patient shows an initial period of pyrexia from 100 to 104° F. which usually lasts for 2 or 3 days. This is followed by a remission over a two-day period. A secondary rise occurs with a remittent fever which may last for several weeks. Following the subsidence of the fever there is a prolonged period of debility which may last for 3 to 6 months. The signs elicited depend on the portal of entry and the patient's reaction to the infection.

The most common form, which accounts for 85% of reported cases, is the ulcero-glandular. It occurred in six of our nine cases. A papule develops at the site of infection. This becomes necrotic and forms a punched out ulcer. Lymphangitis develops with enlargement of the regional lymph nodes. Suppuration of the involved nodes is common. The spleen is not usually palpable.

The oculo-glandular type is much less common, accounting for only about 5% of cases. It occurred in one of our nine cases. The primary lesion is in the conjunctiva. There is a unilateral or bilateral conjunctivitis with swelling of the pre-auricular and anterior lymph nodes. This may be a severe form of the disease. Our patient developed a complicating meningitis and encephalitis with a fatal outcome.

The glandular form of the disease is characterized by enlargement of regional lymph nodes but without a lesion at the site of infection. One of our cases showing unilateral axillary lymph node enlargement falls in this group.

The typhoidal type shows neither evidence of a primary lesion nor regional lymph node enlargement. There is pyrexia with profound prostration and usually a fatal outcome.

The ingestion type is seldom met with. There is a history of eating infected rabbit meat with the constitutional symptoms and laboratory findings of tularæmia. These cases also usually have a fatal outcome.

The diagnosis of tularæmia rarely presents difficulties. A history of having skinned a wild rabbit or having been bitten by a tick or horse fly with a primary skin or conjunctival lesion associated with regional lymphadenitis and prolonged pyrexia points to the disease.

Confirmation by laboratory investigation is of value in diagnosis. The *Bacterium tularense* can usually be grown from smears made from the primary lesion or on blood culture during the first week of the disease. The material, however, has to be inoculated into a guinea pig before it can be cultured on appropriate laboratory media. Agglutinins appear in the blood after the first week of the disease and persist for many years. Agglutination in dilution of 1 in 400 to 1 in 12,800 occurred in our series of cases.

Complications are often met with. Suppuration of the affected lymph nodes, broncho-

pneumonia, pleurisy with effusion, meningitis and encephalitis occurred in our series of nine cases.

The ultimate prognosis is good in most patients but the patient must be warned to expect a prolonged period of debility lasting for months. The mortality in a large series of cases is given as 4 to 5%. This is much higher in the septicæmic form of the disease and in the presence of such complications as pneumonia and meningitis. Three of our nine cases died, one with a complicating meningitis and encephalitis and two with broncho-pneumonia.

TABLE I.

CASES OF TULARÆMIA ADMITTED TO UNIVERSITY HOSPITAL 1931-1944

Source of infection	*Site of primary lesion*	*Type*	*Incubation period*	*Bacterial findings*	*Agglutinin tests*	*Complications*	*Result*
Rabbit	Not determined	Not determined	Not determined	Culture from pleural fluid	1:10,000	Pleurisy with effusion	Recovery
Rabbit	Finger	Ulcero-glandular	Not determined		1:800	None	Recovery
Rabbit	Finger	Ulcero-glandular	3 days	Blood culture negative	1:1,600	Axillary abscess	Recovery
Cat bite	Thumb	Ulcero-glandular	4 days	Blood culture negative	1:1,600	Axillary abscess	Recovery
Not determined	Finger	Ulcero-glandular	Not determined	Culture not done	1:800	Axillary abscess	Recovery
Not determined	Finger	Ulcero-glandular	Not determined	Positive blood culture at autopsy	1:12,800	Broncho-pneumonia	Death
Cat bite	Finger	Ulcero-glandular	36 hours	Blood culture negative	1:800	Broncho pneumonia, pleurisy with effusion, peritonitis	Death
Rabbit	Conjunctiva	Oculo-glandular	Not determined	Positive cultures from cerebro-spinal fluid and blood	1:3,200	Meningitis encephalitis, broncho-pneumonia	Death
Muskrat	None	Glandular	Not determined	Culture not done	1:400	None	Recovery

Prophylaxis and treatment.—Individuals who handle wild rabbits should be urged to wear rubber gloves and to protect their eyes from contamination by infected material.

Many agents have been used in the treatment of tularæmia. Organic arsenicals, the sulfonamides, penicillin and immune serum have been tried without convincing therapeutic effects. Within the past year however, evidence has been advanced by Heilman[5] that streptomycin protects guinea pigs inoculated with lethal doses of *B. tularense*. Foshay and Pasternack,[6] a few months ago published convincing evidence of the value of streptomycin in the treatment of seven cases of tularæmia.

We have not had an opportunity to use this antibiotic in any of our cases in the University of Alberta Hospital. The results of further use of streptomycin in tularæmia will be of great interest.

SUMMARY

The essential clinical features of tularæmia have been outlined.

The frequency of this disease in individuals handling wild rabbits has been noted.

A series of nine cases of the disease showing a mortality of 33 1/3% has been presented.

Experimental and clinical observations would indicate that streptomycin will prove an effective therapeutic agent in tularæmia.

Our thanks are due to the members of the attending staff of the University Hospital who allowed us to publish data on a number of these cases.

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