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## MELIOIDOSIS: SOURCES AND POTENTIAL

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### Introduction

Nearly 60 years ago Whitmore described melioidosis in man in Rangoon.<sup>30</sup> He began his original report with, "The opportunities of a pathologist at a large Eastern Hospital are many; but his time for research work is short, and his conveniences are few." Many of you today may feel akin to Whitmore.

For a long time Whitmore's disease was thought to be an occasional interesting clinical entity in man in Southeast Asia. However, recent events are forcing a change in outlook. Melioidosis is an important disease among troops in Viet Nam.<sup>22</sup> The case-fatality rate is high; the organism is resistant to antibiotic treatment, and many soldiers return to the U.S. to be hospitalized for long periods with a disease usually resembling pulmonary tuberculosis.

The Weekly Morbidity and Mortality Report from the National Communicable Disease Center for May 10, 1969, mentioned isolation of *Pseudomonas pseudomallei* from a stump-tailed macaque monkey (*Macaca speciosa*) imported from Thailand to Holloman Air Force Base, New Mexico. Five other monkeys at the facility had serum titers indicative of infection.

Since World War II there has been a marked increase in international travel. Rapid movement of Americans, both civilian and military, in large numbers has produced many problems related to introduction of exotic diseases. We often fail to realize that there has also been a tremendous increase in shipment of animals. The U.S. Fish and Wildlife Service released the following figures on wildlife importations into the U.S. during 1968: 140,858 mammals (88.3% of which were primates), 492,280 wild birds (not including canaries or psittacines),

and 1,950,091 reptiles. Some of you may feel a little uneasy about the consequences of such importations without adequate safeguards against unwanted introductions into our environment. The question is: Should we be concerned about the possible introduction of *Ps. pseudomallei*?

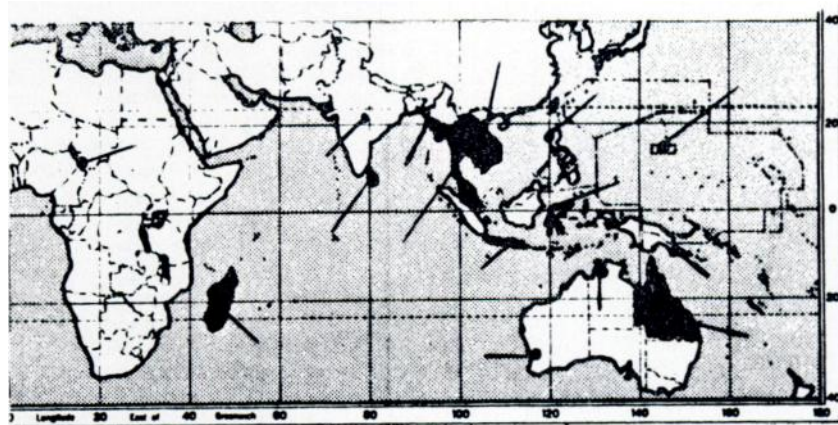
### Enzootic Areas

Redfearn *et al.*<sup>19</sup> suggested that the areas enzootic for melioidosis were to be found between 20°N and 20°S latitude (Figure 1). You will note from the map that the majority of areas do fall in this range, including Southeast Asia, Indonesia, the Philippines,<sup>8</sup> Guam, New Guinea, Ceylon, Chad (Central Africa),<sup>18</sup> parts of Madagascar and Australia, Panama, Aruba, and Ecuador. The extreme exceptions are Nagpur<sup>9</sup> in Central India (21°N), Chittagong<sup>13</sup> in East Pakistan (22°N), and the Chattering Valley<sup>11</sup> near Perth, Australia (between 31° and 32°S). These data are derived primarily from reports of human or animal infection among residents of the respective areas. Two cases in Italians reported by Castellani<sup>2</sup> suggest that there may be other areas as well. One was seen in Libya in 1942 and the other in Italy in 1948. Unfortunately, no geographic history was given.

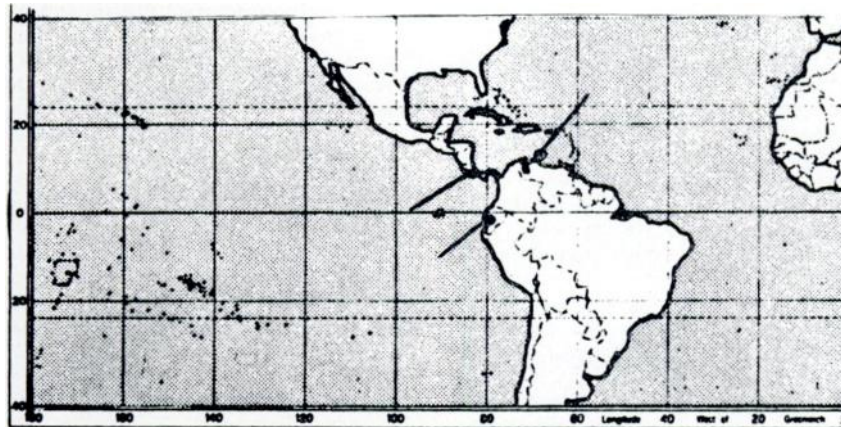
### Animal Hosts

Due to an early report by Stanton and Fletcher<sup>21</sup> in Malaya, melioidosis was thought to be a disease of rodents and occasionally man. French workers<sup>5</sup> in Viet Nam helped to dispel the idea that rats were a significant reservoir when they found only 1 infected among 20,000 examined. There has been a gradual increase in the list of naturally infected

### ENZOOTIC MELIOIDOSIS AREAS



### AFRICA, ASIA, AUSTRALIA, PACIFIC



### CENTRAL AMERICA

FIGURE 1

animals (Table 1). Undoubtedly, there are other species which become infected naturally in addition to the mammals listed.

Abscesses in the lungs, liver and spleen are the most common lesions. The clinical course may be acute to chronic. Losses among sheep in Australia varied from 2.5% to 30%.<sup>3</sup> *Ps. pseudomallei* has been isolated from an aborted goat fetus<sup>20</sup> and normal goat milk.<sup>10</sup> Melioidosis

has been a serious problem in some swine producing areas.

Stanton and Fletcher<sup>25</sup> reported an outbreak in their guinea pig colony in Malaya. To date, the hamster is the most susceptible host tested, with an LD<sub>50</sub> of less than 10 organisms when inoculated intraperitoneally.<sup>11</sup> The weanling Syrian hamster is the animal of choice for inoculation of any suspect material.<sup>7</sup> Death usually occurs in 3 to 5 days.

TABLE 1. *Hosts found infected in nature with Ps. pseudomallei*

1. Man
2. Cat<sup>24</sup>
3. Cow<sup>15</sup>
4. Dog<sup>25</sup>
5. Horse<sup>17</sup>
6. Sheep
7. Swine
8. Domestic goat<sup>16</sup>
9. Wild goat  
(*Capricornis sumatrensis*)<sup>17</sup>
10. Orang-Outang (*Simia satyrus*)<sup>20</sup>
11. Macaque monkey (*Macaca sp.*)<sup>21</sup>
12. Stump-tailed macaque  
(*Macaca speciosa*)
13. Tree climbing kangaroo  
(*Dendrolagus sp.*)<sup>6</sup>
14. Wild rat (*Mus griseiventer*)<sup>21</sup>
15. Rat (*Rattus norvegicus?*)<sup>2</sup>

#### Agent and Reservoir

The causative agent of melioidosis was known for years as *Malleomyces pseudomallei* and is closely related to the glanders agent. In fact, one name given to melioidosis was pseudo-glanders. Due to the work of Redfean<sup>19</sup> and Stanier,<sup>23</sup> these agents are now classified in the genus *Pseudomonas*. Lack of motility in the glanders agent, *Ps. mallei*, is the chief difference between it and *Ps. pseudomallei*.

As was mentioned earlier, melioidosis was thought to be a true zoonosis with rodents as the probable reservoir. Studies in Viet Nam, Australia,<sup>12</sup> and Malaya<sup>27</sup> have concluded that *Ps. pseudomallei* actually survives and multiplies in the soil and/or water. Using hamster inoculation, *Ps. pseudomallei* has been isolated from surface water specimens from sites throughout Malaya.<sup>27</sup>

Isolation was least frequent from specimens collected in primary forest (approximately 1%) and most frequent from wet rice fields (15 to 33%). Generally, isolation was more successful from water than soil. However, the exception was soil from cleared, grassy fields used for athletics, livestock grazing, etc. with the percent positive varying from 15 to 28.

#### Transmission and Detection of Infection

Entry through abraded skin is, perhaps, the most common route of transmission. Local abscesses are often seen in man, particularly on the legs. It is still unclear whether localization in the lungs in naturally infected cases is usually due to inhalation or spread via the bloodstream. Both can occur. Infection by the oral route can be produced experimentally.<sup>14</sup> Transmission from animal to animal is apparently quite rare.

An indirect hemagglutination test has been developed which provides a rapid, simple, and accurate method for the detection of serum antibodies. Serum surveys of native human populations in Southeast Asia indicate that inapparent (or at least very mild) infection is common.<sup>20</sup> Populations in rice growing areas had the highest % positive sera. The hemagglutination test has been shown to be useful in detecting infection in sheep and goats. However, results of surveys of wildlife sera have not been reported. The micro-titer method is applicable. Thus, a very small amount of serum is needed which is often a necessity in wildlife studies.

#### Current Questions

To summarize our present knowledge:

1. Melioidosis occurs naturally in tropical areas throughout the world. Human and animal cases returning from these areas are being seen with increasing frequency in the U.S.
2. A variety of mammals can be infected and the disease is extremely resistant to treatment.
3. *Ps. pseudomallei* resides in the soil which seems to be the reservoir for virtually all animal infection.

To answer the question, "Should we be concerned?" I would say "yes" until we have sufficient evidence to the contrary. We need to know more about the micro-environment in which the organism survives before we will know whether soils in some tropical and semi-tropical areas of the U.S. are susceptible to colonization. Growth occurs between 5° and 42°C and under some strictly anaerobic

robic conditions.<sup>19</sup> Abundant moisture seems to be required, but it is not known how well it will survive in nature under temporary drought conditions. It is possible that an imported wildlife species harboring chronic infection might be a source of soil contamination when placed in a natural enclosure such as those used at present in Florida (Ex. Africa, U.S.A.). Of course, this is true for domestic species as well.

The limits of enzootic areas need to be determined. In particular, there are questions concerning several areas in the Western Hemisphere. Panama<sup>10</sup> and Ecuador<sup>1</sup> are suspected due to reports of individual human cases with good histories incriminating the respective locations. No ecologic work has been done in these 2 countries. The island of Aruba has a single report of disease in domestic animals.<sup>28</sup> There is some question in the latter instance whether or not these animals were imported from an enzootic area. No follow-up study has been reported. Tools which should aid in an-

swering these questions<sup>26,27</sup> are surveys of sera from domestic and wild mammals followed by isolation attempts from the environment where serologic evidence indicates infection has existed.

Equally important questions remain concerning animal hosts as potential sources of environmental contamination. Among known susceptible hosts, how likely is urinary or fecal excretion in any stage of infection? Would the decomposing carcass of an infected animal be a good source?

What other hosts are likely to be found infected naturally? The number of experimental infections reported are few. Stanton and Fletcher infected experimentally a cynomolgus monkey (*Macacus cynomolgus*).<sup>21</sup> On the other hand, they said domestic fowl were not susceptible.<sup>21</sup> An organism such as *Ps. pseudomallei* might find a good home in lower vertebrates or even invertebrates.

When these questions are answered, our concern may have just begun.

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