

STUDY OF 72 CASES OF HUMAN BRUCELLOSIS IN TEHRAN

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Although for lack of attention, cases of human Brucellosis in Tehran remained undiagnosed until twenty five years ago, (1) the disease has been in existence in Iran since earliest times; Spink (1956) postulates in fact that it was the importation of Iranian goats to the island of Malta which was responsible for the disease introduction there.

Today Brucellosis is endemic in most parts of Iran. It is the more limited scope of this paper however to present a survey of the illness in Tehran.

According to the published reports of the Public Health and Veterinary Departments, the disease is prevalent among cattle, goats and sheep in most of the country. The degree of incidence and the species of animal affected vary from area to area. The highest levels of contamination are to be found in Tehran (cattle) and in Isfahan and Neishabour (goats).

Of the three species of *Brucella*, it is *Brucella abortus bovis* which is the casual agent in infecting Iranian cattle and *Brucella melitensis* which infects goats.

Human Brucellosis, too, varies in incidence and severity from area to area. In general, *Br. melitensis* produces a more severe illness than *Br. suis* or *Br. abortus*, (the least severe of the three). With the exception of one case due to *Br. abortus*, recorded by Dr. F. Motazedi in Medical Ward of Pahlavi Hospital in 1961, all the cases of human Brucellosis in Tehran were caused by *Br. melitensis*. The Public Health Department reports from other cities would seem to confirm the above proportion. In the blood cultures which were performed on all our 72 cases, the disease was shown to be due to *Br. melitensis*.

1 - Dr. Abbas Adham recorded for the first time the presence of human Brucellosis in Tehran

The cases of human Brucellosis which are admitted to the 100 bed infectious diseases department of Pahlavi Hospital are from the Tehran city and its suburban area. They constitute approximately one percent of the 2,000 patients admitted yearly in this department. During the last five years we have had 72 cases in which the initial diagnosis of Brucellosis was confirmed by clinical and laboratory findings.

Analysis of Data

In our seventy-two cases the following data were compiled and compared with classical descriptions of the illness and with comparable data concerning foreign patients.

1. Age group and incidence
2. Sex incidence
3. Seasonal incidence
4. Occupational relationship and incidence
5. Clinical signs and physical findings
6. Laboratory findings
7. Epidemiology and mode of transmission
8. Treatment

Discussion

1. Age Incidence: Infants and children seem to be more resistant to Brucellosis, or manifest the disease in an undiagnosed transient form. In our 72 cases the age incidence was as follows:-

Table 1 - Age incidence

<u>Age</u>	<u>Percentage</u>
Under 10 years old	None
10 to 20	29.2
20 to 40	61.1
Over 40	9.7

As table 1 indicates, most of the patients are between the years of 20 and 40, the most active years of life, and hence the time when people are most exposed to infection. In the Pediatric Ward of Pahlavi Hospital and in the Children's Section of our department there has not been a proved case of Brucellosis in any patient under the age of 10.

2. Sex Incidence. In our 72 cases, the sex incidence was as follows:

Table 2- Sex incidence

<u>Sex</u>	<u>No</u>	<u>Percentage</u>
Male	49	68.0
Female	23	32.0
<u>Total</u>	<u>72</u>	

Since most of the milk handling in Iran is done by women the lower percentage of illness among them might suggest that direct contact and cutaneous inoculation may not be the principal methods of transmission of the disease. It is the men, whose jobs and social activities take them outside of the home and who are thus more exposed to infective sources that contract the illness 68% of the time.

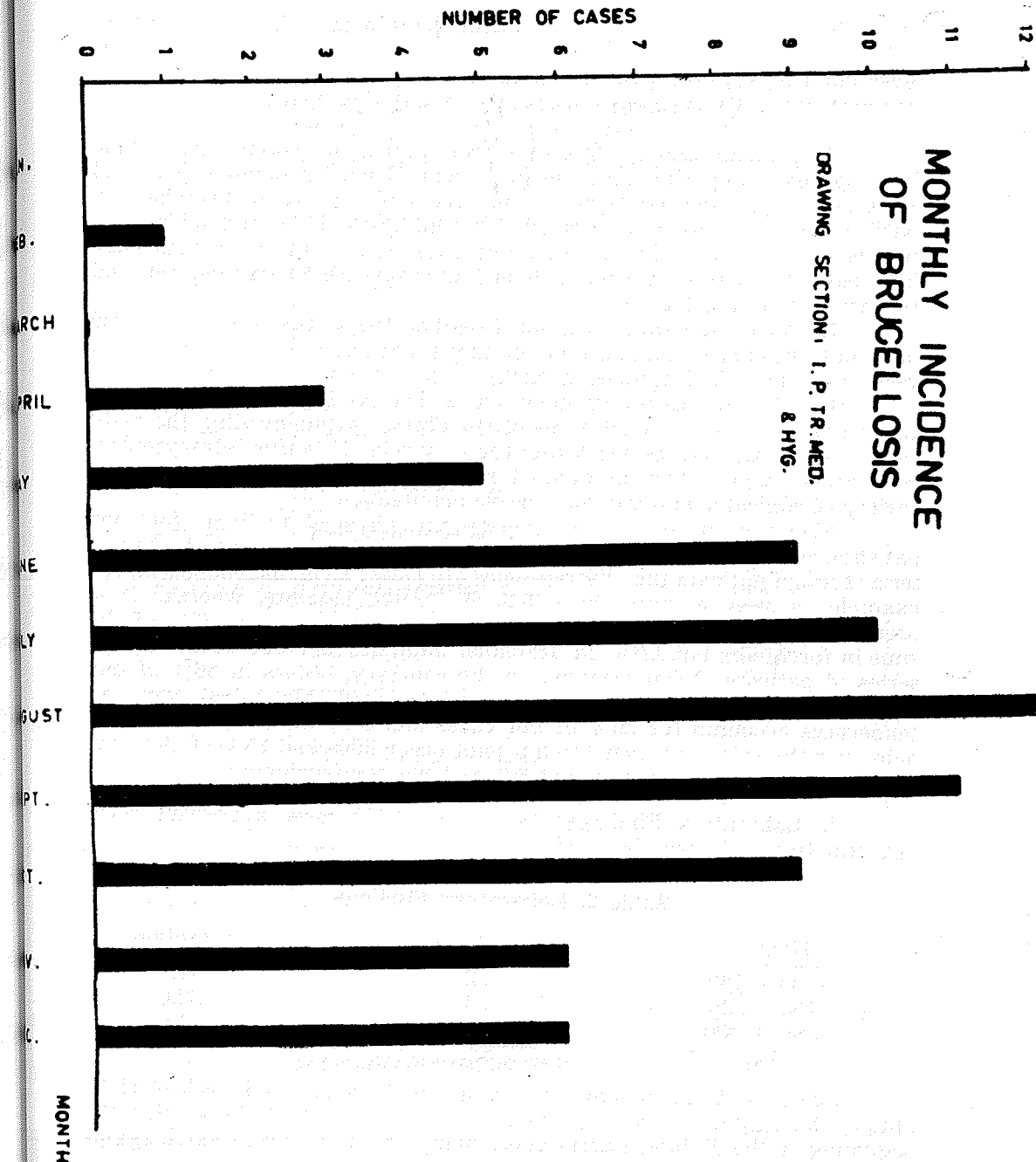
3. Seasonal Incidence: The Brucellosis cycle begins in the spring months, reaches its peak in the summer and declines during the autumn months to zero in the winter, (graph 1). This should be noted in relation to an epidemiological point to be raised later.

4. Occupational Relationship and Incidence: According to the classical descriptions, Brucellosis is primarily a disease involving the rural population rather than city dwellers and occurring most often in those who have an occupational contact with the infected animals or their products. In our series, however, we could only find 7 cases in which there was an occupational relationship (9.3%). This lack of correlation and the low incidence of the disease among females-the dairy workers- (pointed out in Table 2) may imply that direct contact with the infected animals and their products may not be the main route of transmission.

5. Symptomatology: Brucellosis is an infectious disease with a variety of clinical manifestations. In fact, one can state, that all the symptoms which are present in the usual infectious diseases are found in Brucellosis. It may have an abrupt onset, indistinguishable from many other infections, or it may begin insidiously with vague and misleading symptoms, which make it difficult to diagnose. Frequently only after days or weeks and with the aid of laboratory test will diagnosis be possible. In all of our cases the clinical manifestations of the illness suggested the presence of Brucellosis, with the exception of one patient who suffered from orchitis without any attendant illness of fever, but who on further investigation showed a positive agglutination test with a titer of 1/640.

Since there are some discrepancies between the symptoms and signs of Brucellosis which are described in classical medical books and those seen in our patients, we shall give some further details about what we observed:

a) Subjective symptoms: Rarely do we have two similar cases. Patients complain of chill, fever, weakness, anorexia, general body pain, sweat, headache, backache, pain in the joints, nervousness, depression, pain in the back of the neck, abdominal pain, coughing, constipation, diarrhea, nausea, vomiting and a variety of neuralgias as well as genito-urinary disturbances. The number and severity of the symptoms about which the patient complains, varies from case to case. In the graph 2 the symptoms presented by our patients are compared with those of foreign records. The comparison indicate that while foreigners complain more of sweat, weakness, headache, cough, nervousness, anorexia and depression,



our patients complain mostly of backache, pain in the joints, constipation and genito-urinary disturbances. (We had one patient who was free of fever but who suffered pain in his bones and joints. When myelo-culture was performed, *Br. melitensis* was isolated and identified).

b) Physical findings, too, vary from patient to patient and include fever, lymphadenopathia, splenomegalia, skin lesions, abdominal pain and tenderness, pain and tenderness over the spine, nervous disturbances, cardiac disorders, orchitis, pain over the hip joint, bone and joint pain, anemia, and jaundice. The severity and character of these findings vary from patient to patient for instance one may have an enlarged spleen and another only a palpable one.

Nor does temperature exhibit a regular shape: Some patients show the remittant curve, others the undulating type; and one of the patient as mentioned above had no fever at all.

Brucella do possess an endotoxin which participates in the pathogenesis and clinical manifestations of the illness. After invading the body tissues, the organism resides within the host cells. It is this intracytoplasmic parasitization which accounts for the chronicity as well as for the variety of clinical symptoms the disease manifests.

When, in graph 3, we compare the physical findings for our patients, with those which are described in medical books or which characterize foreign patients the discrepancies are clear; Lymphadenopathia, for example, is seen in more than 45% of foreign patients, whereas it is present in only 26% of our patients. Liver enlargement occurs 25% of the time in foreigners but 17% in Iranians. Jaundice did not occur in our series of patients. Splenomegalia, on the contrary, occurs in 66% of our patients, but in only 44% of foreign patients while abdominal pain and tenderness accounts for 20% of our cases and only 8.5% of theirs; and pain over the spine and over the hip joint occur 36% and 25% of the time respectively for our patients, and 6% and 3% for foreigners.

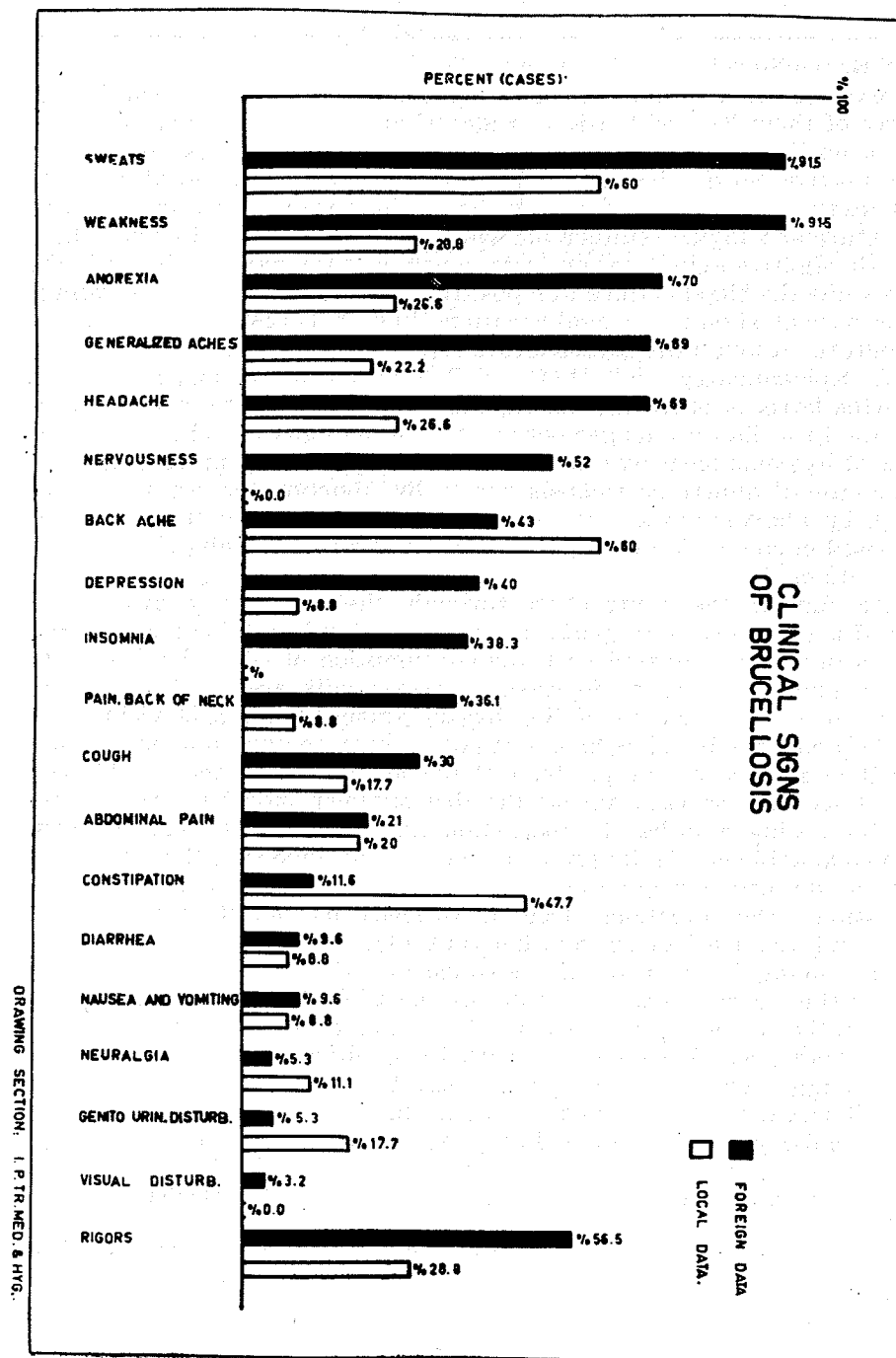
6. Laboratory Findings: In 70 out of 72 cases a positive sero-agglutination test was observed.

Table 3. Laboratory Findings

Titer	No. of Cases	Percentage
1/80-1/160	22	32.0
1/160-1/320	22	32.0
Over 1/320	26	36.0
Total	70	

Since all of our patients were admitted in the second week of their illness, the agglutination test was performed at least 10 days after the beginning of the disease. Furthermore many cases had progressive agglutination titers.

Blood Culture: In our series, of 50 blood cultures performed 16



cases of *Br. melitensis* were identified, (32%).

Myeloculture: In our series, 12 myelocultures were performed and in 6 cases of them *Br. melitensis* was identified. Ten of these twelve cases showed a positive agglutination test as well and four of these ten cases showed positive blood cultures and four showed positive myelocultures. It is interesting to note that whenever the agglutination test was positive, blood culture and myelo - culture did yield the same results. In two other cases with negative agglutination tests, myelo-culture was positive in both of them while the blood culture was positive in only one. In one interesting case the patient showed an agglutination titer of 1/1280 and a positive blood culture although the myeloculture remained negative.

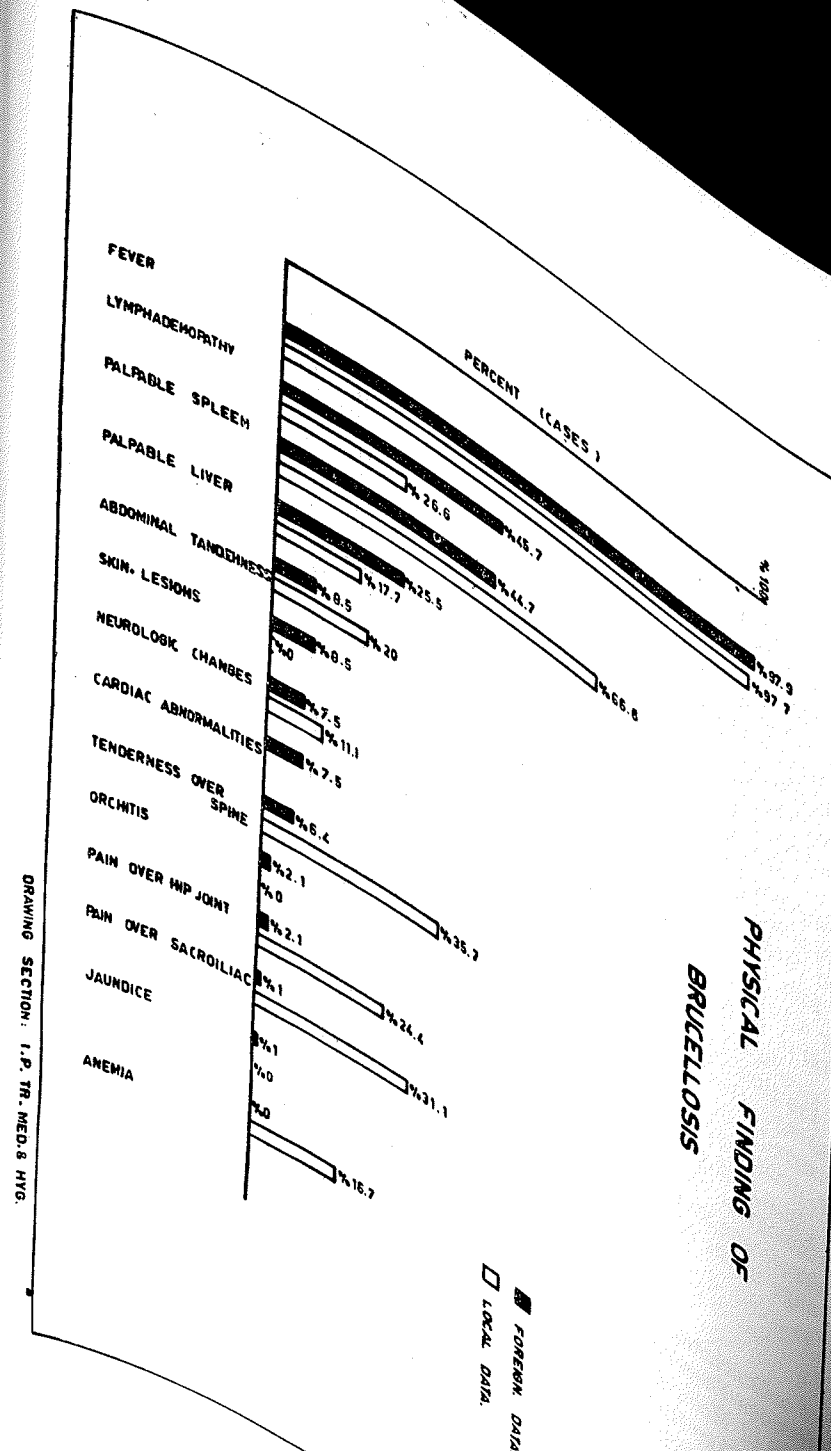
7. Epidemiology and Mode of Transmission: Considering that *Br. abortus bovis* is prevalent among the cattle of the Tehran area, who excrete the *Brucella* for a longer period of time than goats, and considering the lack of hygienic measures in the cow-sheds, it is most interesting that only one case of human Brucellosis due to *Br. abortus* was reported. Apparently, *Br. abortus* has a very low pathogenic potency for Iranians, and as discussed in connection with parts 2 and 4, exhibits a negligible occupational relationship.

As far as the contraction through the alimentary system is concerned the proportion of goats' milk or goats' milk products consumed in the Tehran area compared with the consumption of cows' milk is very low; even children who are deprived of breast milk are fed cows' milk. However since the incidence of the disease among children is almost nil (Table 1), and since *Br. abortus* is virtually absent among humans in Iran, despite the quantity of milk products they consume, and since the disease occurs at its highest rate during the dry summer months rather than during the spring months of procreation among sheep and cattle when there is an abundance of milk products, we can conclude that the transmission of the disease through the digestive tract is not the main route of transmission, (the infectious dose of *Brucella* by mouth remains unknown), and we must look for another route(1).

In looking for a mode of transmission other than that of direct contact or the digestive tract, we note that small flocks of sheep and goats are constantly moving from one part of the city to another on their way to sale or transport. Goats infected with *Br. melitensis* excrete the casual agent through their urine into the streets. This pathogenic agent, after drying will mix with the dust and air and in this form enter the respiratory system. Similarly in Isfahan and Fars, the herds of the tribes, travelling back and forth from their summer and winter quarters in the company of their animals would be responsible for the spreading of *Brucella* through the air.

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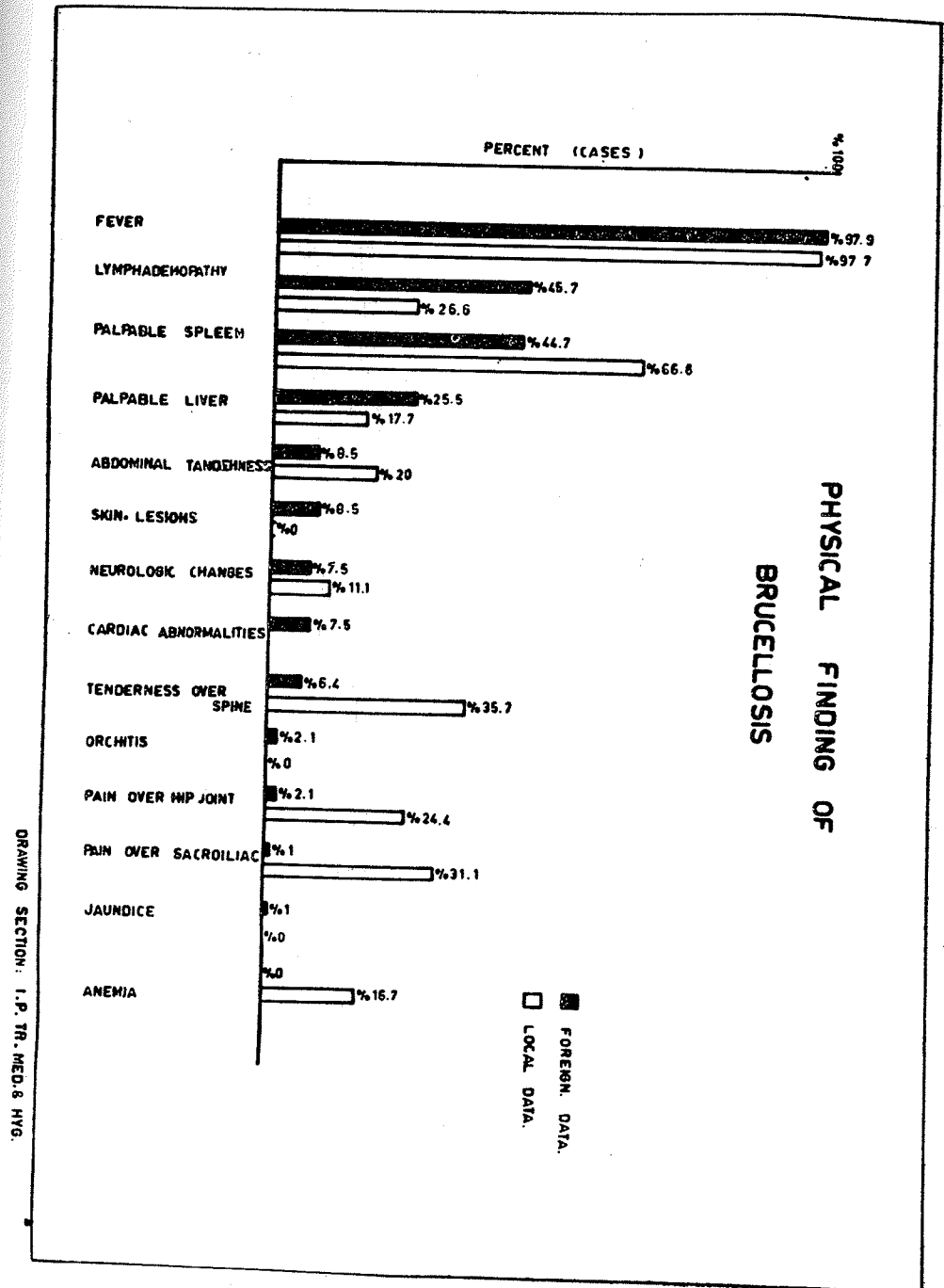
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during the dry summer months, we suggest that, in addition to the other routes of transmission, Brucellosis may be an air-borne disease contracted through the respiratory system.

8. Treatment: The chronicity of the disease, the administration of unsuitable therapy in treating the disease in the diagnosed cases, and hence the use of a variety of drugs for this purpose create tremendous problems in the treatment of Brucellosis. In our cases we usually used trade names of Tetracycline derivative, Sulfonamides, and Streptomycin. In acute cases we had best results with an association of Tetracycline with Sulfonamide or Streptomycin. In chronic cases best results were obtained from the use of all three in association. In these cases, however, we observed a few relapses.

We treated five cases with chloramphenicol succinate in high dosages according to the following schedule; one successfully treated case was given 5 grs. of chloramphenicol parenterally for a period of ten days, and then a dose of 2 or 3 grs, daily until a total of 60 grs. was reached. In four other cases the drug was administered in dosages of 6 grs. daily for a period of 5 days and was continued with 4, 3, 2, grs. daily until a total of 50 grs. was reached.

In one of the above cases the patient's blood culture was negative at the time of his admission but his myeloculture was positive (**Br. melitensis**). One month after therapy with Chloramphenicol the illness recurred. At that time the patient's blood culture was positive and **Br. melitensis** was isolated and identified.

All of the above cases were under myelogram control to note any pathological change of the blood if it occurred. In one case the bone marrow was studied over a period of six months. We found no pathological change in the blood and no alveoli in the red cells.

Summary and Conclusions:

Conclusions based on 72 proven cases of Brucellosis observed at the Infectious Diseases Department of Pahlavi Hospital, Tehran University, School of Medicine from 1958-1962 are as follow:-

1. Age Incidence: Highest between the ages of 20 to 40.
2. Seasonal Incidence: Highest during the summer months.
3. Occupational Relationship and Incidence: In 90% of the cases, there was no contact between the patients and the infected animals or their products.
4. Sex Incidence: The majority of our cases, (68.0%) were men.
5. Despite the prevalence of **Br. abortus** among the cattle of the Tehran area, human Brucellosis due to **Br. abortus** is rare. All the reported cases were due to **Br. melitensis**.
6. The difference between the symptomatology in our cases and those of foreigners are described. They may be due to the difference in the casual agent and to the difference in living conditions in Iran.

7. The Incidence of Brucellosis in children is extremely low. This may be due to their natural resistance and to their more limited living conditions.
8. The disease is almost absent in occupationally exposed people, despite the number of infected cattle in the Tehran area. This may be due to the low pathogenic potency of **Br. abortus** in Iran.
9. Mode of Transmission: Not discounting the possibility of transmission through the alimentary tract, we suggest that *Brucella* excreted by the goats kept in the city or those which belong to the tribes who pass some times during winter and summer movement in the cities, may mix with the dust and air and so gain entrance to the respiratory system.
10. Therapy: Best results in chronic cases were obtained through an association of Tetracycline derivative with Sulfonamides and Streptomycin. Chloramphenicol has yielded good results, although in some cases the illness may recur.

Résumé

Les conclusions appuyées par des observations se rapportant au 72 cas confirmés de Brucellose étudiés dans les Services de Maladies Infectieuses de l'Hôpital Pahlavi de la Faculté de Médecine de Téhéran depuis 1958 jusqu' à 1962 s'énoncent ainsi:

- 1 - Incidence de l'âge: plus fréquente entre 20-40 ans.
- 2 - Incidence saisonnière: plus fréquente pendant les mois d'été.
- 3 - Incidence professionnelle: dans 90% des cas nous avons noté aucun contact entre les patients et les animaux infectés et leur produits.
- 4 - Incidence de sexe: la majorité de nos cas (68%) se rapportaient au sexe masculin.
- 5 - Malgré la grande fréquence de *Br. abortus* parmi le cheptel de la région de Téhéran des cas humains de Brucellose dus à ce bactérie sont très rares. Tous les cas observés étaient dus à *Br. melitensis*.
- 6 - La différence entre la symptomatologie des cas observés par nous et ceux à l'étranger sont décrites dans cet article. Elles sont dues probablement aux différences entre les agents causaux de même qu'aux conditions de vie en Iran.
- 7 - Incidence de Brucellose parmi les enfants à bas âge est extrêmement basse. Ceci est probablement dû à leur résistance naturelle et à leur conditions de vie assez fermées.
- 8 - La maladie est à peu près absente parmi les gens dont la profession les expose à cette maladie et ceci malgré le nombre de cheptel infecté dans la région de Téhéran; ce fait peut être dû à la faible virulence de *Br. abortus* en Iran.
- 9 - Mode de transmission: En n'éliminant pas la possibilité de transmission par voie digestive nous pensons que les *brucella* excrétés par les chèvres élevés dans les étables urbains ou bien celles traversant les villes par des tribus nomades pendant leur transhumance, peuvent se mélanger à l'air et à la poussière gagnant ainsi le système respiratoire de l'homme.
- 10 - Traitement: Les meilleurs résultats ont été obtenus dans les cas chroniques par l'association de dérivés de Tétracycline avec Sulfonamides et Streptomycine. La Chloramphenicol a donné de bons résultats sauf dans quelques cas où nous avons observés des rechutes.

References

- 1 - Spink, W.W. 1956. The nature of Brucellosis. University of Minnesota Press.
- 2 - Ministry of Health of Iran, Department of Public Health. 1962 A report on Brucellosis in Iran.
- 3 - Ministry of Agriculture of Iran. 1962 Report of Brucellosis.
- 4 - Lancet 1962. Annotations: Undulant Fevers, Lancet, 11, 923.

References

- 1 - Spink, W.W. 1956. The nature of Brucellosis.
University of Minnesota Press.
- 2 - Ministry of Health of Iran, Department of Public Health. 1962
A report on Brucellosis in Iran.
- 3 - Ministry of Agriculture of Iran. 1962
Report of Brucellosis.
- 4 - Lancet 1962. Annotations: Undulant Fevers, Lancet, 11, 923.