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Clinical Forms of Brucellosis and Their Treatment (A Methodological Note).

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The basic achievements in the modern study of brucellosis are the result of works by our native investigators (P. F. Zdrovskiy and his pupils, N. N. Stepanov, G. P. Rudnev, A. L. Myasnikov, G. N. Udintsev, N. I. Bagona, I. L. Bogdanov, N. D. Beklemishev, and others).

A valuable store of information on the brucellosis problem was created by the scientific and practical workers of Siberia (B. P. Pervushin, G. A. Fandikov, I. S. Novitskiy, G. F. Barbanchik, O. D. Sokolova-Ponomareva, A. N. Tselishchev, et al). Nevertheless, in spite of the important successes in this regard, many sides of this problem cannot be considered as resolved; this applies particularly to the treatment of brucellosis.

Brucellosis in man is distinguished from other specific infections by a large variety of both clinical and pathomorphological manifestations. Being a chronic infectious illness, it afflicts various organs and systems.

A peculiarity of the clinic of brucellosis is the undulating course with its periods of aggravation and periods of more or less protracted abatement. Brucellosis, as a rule, takes a prolonged course and often can lead to prolonged incapacitation and sometimes invalidism. This infection rarely takes an abortive course.

The variety of clinical manifestations of brucellosis is related to many factors (the character of the pathogen, the reactivity of the macroorganism, the phase of the illness, etc.).

Many investigators (I. S. Novitskiy, T. Kh. Madshiddinov, N. I. Bagona, O. D. Sokolova-Ponomareva et al) refer brucellosis to the category of infections having a cyclic course, which depends on the phase of the disease and the reactivity of the patient's organism. G. P. Rudnev and others consider that the cyclic course is not characteristic for brucellosis, nor for any process of a septic nature, but, on the contrary, that the acyclic course is typical

for it. He, at the same time, acknowledges that the absence of a cyclic nature by no means indicates an absence of pathogenic mechanisms in the development of brucellosis. This "clause" of G. P. Rudnev's, so it seems to us, draws together the differing, at first sight, viewpoints of the investigators.

It is indisputable that brucellosis of man occurs with the development of distinct forms and phases of the disease that are distinguished from each other by their clinical, pathogenic and immunobiological peculiarities.

As the observations of many authors (V. A. Gramenitskiy, A. L. Katsenovich, N. T. Gretsova et al) prove, the different clinical manifestations of the brucellosis infection depend to a certain degree on the type of pathogen. 113

It is well known that the illness caused by the Malta micrococcus develops acutely, in the majority of cases, as an over-all generalized infection with a further transition into a chronic form (secondary-chronic brucellosis according to Bagosa).

In cases of brucellosis related to infection of large horned cattle and swine by brucella, the disease develops gradually and takes a chronic lingering course (primary-chronic brucellosis).

With the Malta variant, however, an acute period does not always occur in the development of the disease, whereas, in some cases it is possible to observe an acute course with the sporadic brucellosis also.

As is known, in the conditions of Omsk Oblast the brucellosis is the Malta variant; meanwhile, as the materials of our clinic attest (K. K. Yushkevich), we have failed in approximately 15 % of all cases of brucellosis to clinically detect an acute period and the development of the disease bore a character of primary-chronic brucellosis from the very start.

The observations of G. F. Barbanchik, A. A. Morkinskaya, V. P. Putalovaya et al., show that in Omsk Oblast, where brucellosis illnesses are caused chiefly by the Malta micrococcus, the disease takes a more severe course than in the cases where the brucellosis is caused by brucella of large horned cattle. In particular, with the Malta variant, lesions of the cardiovascular system emerge more regularly than with infection by Bang's brucella.

While noting the significance of the pathogenic properties of the pathogen, it should be emphasized that in brucellosis, as in other infections, in the development of the disease, during its course, and also in the termination, the most important role belongs to the macroorganism, the importance of which has been underrated in the recent past by some investigators.

In speaking of the leading role of the macroorganism, one should not, as an inference of what has been presented above, minimize the importance of the pathogenic properties of the brucellosis pathogen as a specific infectious factor. And, at the same time, one should not reduce the entire problem of brucellosis as a disease to only the presence of the pathogen in an organism, but such tendencies do occur in the literature.

The presence of the pathogen in the organism is not always manifested by any clinical symptoms that would indicate the disease. On the other hand the disappearance of the pathogen from the organism of a patient still gives no basis to speak of his recovery from brucellosis.

The question about the duration of the pathogen's attendance in the organism is connected by some authors to the question of the continuance of the brucellosis illness in animals and man. During recent times this problem has attracted the particular attention of many investigators. The observations of P. F. Zdrovovskiy, V. A. Shtriter, V. N. Nikolayev, R. A. Tsion et al, have showed that in animals, both in experiment and in conditions of natural infection, there comes not only a clinical but also a bacteriological recovery within various time periods after the initial infection (from 6 to 24 months).

The data in the literature concerning the continuance of brucellosis in man are contradictory. Basset-Smith considers that the average continuance of epidemic brucellosis is 4 months; according to the findings of A. Hardy and Jordan, it was 3 months. The observations of G. A. Pandikov on 150 brucellosis patients showed that there were neither exacerbation nor relapse in them during a period of from 2 to 10 years. G. I. Grinberg thinks that recurrent generalizations of the brucellosis process are conceivable only for a period of 1½-2 years after the time of illness and that after this only the para-allergic (nonspecific) post-brucellosis illnesses can occur.

Our observations on brucellosis patients (approx. 1,000 patients) show that some clinical manifestations of the disease can be encountered for 5-10 years after the initial infection. ~~By this we do not refer to the residual non-reversible changes that have a stable character and develop as a result of sclerofibrous processes, but rather to reversible symptoms (temperature reaction; accelerated erythrocytic sedimentation rate; changes on the part of the support-motor apparatus - polyarthritis, spondylosis, etc.).~~

In some of the cases, with the presence of some brucellosis manifestations, we speak of reinfection. Reinfection is possible, both in animals and in humans. V. A. Nikolayev indicates that one often encounters repeated outbreaks of brucellosis in animals. Reinfection is the source of these outbreaks more frequently than relapse. G. I. Grinberg speaks about reinfection of man.

We also had certain grounds to speak of reinfection in many cases of brucellosis. The following data indicated reinfection rather than relapse:

1. The detection of any disease symptoms developing 5-10 years after the initial infection by brucellosis and which characterize the acute or subacute period of the disease.
2. A manifestation by the agglutination test that is not characteristic of brucellosis in the late period of the disease's development.
3. A positive blood culture in isolated cases. Although, as has been stated, very often in the late periods from the start of the initial infection there are symptoms observed that are intrinsic to chronic brucellosis.

Our material confirms the existent detailed observations of B. P. Pervushin et al. concerning the fact that within three years after infection it is impossible to receive a positive blood culture, unless there is a reinfection.

The question then arises - is it possible to speak of self-healing within 2-3 years from the start of the illness, or do grounds exist at a later period in many of the cases to regard any symptoms as manifestations of brucellosis, although brucella might not be detected in the person's organism.

For a proper understanding of this question it is applicable and necessary for a person to consider the complex effect of three factors in the development of brucellosis: the infectious (the pathogen), the toxic and the allergic. It is indisputable that at the start of the illness a special role is played by the microbic (infectious) and toxic factors, and in the later periods - by the allergic, whose importance can increase upon the transition of the disease into the chronic form. Whereupon, in a later period the latter is often the main factor.

In the early period of the illness's development the brucella and their toxic products, while circulating in the blood (bacteremia and toxemia), create conditions for the manifestations in a form of over-all infection (primary generalization). At this stage, death of the brucella and recovery can occur as a result of the action of the protective factors of the macro-organism. In the majority of cases, however, the pathogen remains in the organism upon the abatement of the acute period, causing endogenic, oft-repeating generalizations, which cause the appearance of the allergic reactions in the organism as a whole and in its various organs and systems (chronic brucellosis).

In chronic brucellosis, as has been pointed out, there may be an absence of brucella in the organism in the late periods of the illness, but one still cannot speak of self-healing in these cases. Some clinical manifestations of the disease may still be observed for a protracted time after the so-called self-healing.

With the chronic course of the process there is often a hypersensitization that determines the clinic of the illness. Against a background of an hyperergic condition of the organism, any nonspecific agent (microbe, cooling, etc.) can cause an outbreak of the disease. The various actions and irritations attending a predisposition to pathological reactions on the part of the entire organism and the more afflicted organs (i.e., with the presence of persistent residual reactions) can often lead to relapses and exacerbations of brucellosis. In these cases some authors speak of para-allergic (non-specific) post-brucellosis afflictions. In principle this is correct. It must be emphasized, however, that here we are contending with a disease that sometimes lasts many years and not with residual phenomena that require no therapy.

It seems to us that G. P. Budnev is right in pointing out that the pathogenesis of brucellosis in man cannot be regarded primarily from the point of view of the "fate" of the brucella in an organism. The para-allergic (non-specific) post-brucellosis afflictions are, in the majority of cases, active manifestations of chronic brucellosis. Therefore, it seems to us that after

5-10 years, when there are clinical symptoms, it is possible to speak of the brucellosis as an illness. One should differentiate between these manifestations (para-allergic) and the residual brucellosis, in which there are irreversible persistent sequela of the given illness (cirrhoses, scars).

Some investigators justly, in our opinion, point out that hypersensitized persons manifest a particular tendency to secondary infection by brucellosis, which by itself demands some therapeutic measures.

Although in a chronic course of the brucellosis illness it is not easy to demarcate the brucellosis as an active infection from the post-brucellosis changes whose pathogenic basis is a nonspecific irritant in a sensitized organism, nevertheless it is necessary to attempt such a demarcation by using all of the existing diagnostic methods.

It is quite clear that the correct approach to a rational therapy is conceivable only on the basis of the above interpretation of the pathogenesis of any brucellosis manifestations in each individual case.

In the treatment of brucellosis it is necessary to proceed from the clinical picture of the disease and the dynamics of the process (acute, subacute, chronic, residual).

Positive serological and, particularly, allergy tests, without the clinical symptoms of the disease, are not in themselves indications for the use of any sort of therapeutic measures.

As is known, the indicated positive tests show only that a person is infected or just that he has had contact with the brucellosis pathogen, but still do not speak of the clinical presence of the disease.

The proposed classifications of the clinical forms of brucellosis are comparatively many, but to date there is not a single generally-accepted classification.

The following classification of G. P. Rudnev's has received the most wide-spread dissemination. The etiological and pathogenic principles go into the structure of this classification.

Classification of the Clinical Forms of Brucellosis:

A. By the gravity of the disease:

1. Mild
2. Of median gravity
3. Severe

B. By the continuance of the disease:

1. Acute (to 3 months)
2. Subacute (to 6 months)
3. Chronic (exacerbation, relapsing latency)

C. By the patient's condition:

1. Phase of compensation
2. Phase of subcompensation
3. Phase of decompensation

D. By the etiological diagnosis:

1. Brucella of sheep
2. Brucella of swine
3. Brucellosis (pure)

E. By the nosological diagnosis:

1. Brucellosis (pure)
2. Mixed brucellosis (with malaria, dysentery, etc.)

F. By the predominance of afflictions:

Of the support-motor system, neurobrucellosis, etc. (see below)

G. By the outcome and prognosis:

1. Complete recovery
2. Incomplete recovery
3. Vestigial brucellosis (a clinic of the sequela)

Concerning chronic brucellosis, G. P. Budnev and many other authors recommend that the principle of an affliction of some system be adhered to in the classification, indicating that if this principle is less acceptable in the acute and, particularly, subacute brucellosis, then with the chronic forms, as a result of the repeated relapses, the local manifestations become more clearly expressed with each attack.

The classification of chronic brucellosis is presented below.

Classification of Chronic Forms of Brucellosis:

I. Visceral form:

1. Cardiovascular
2. Pulmonary
3. Hepatolienal

II. Osteoarticular or locomotor form:

1. Affliction of the joints
2. Affliction of the bones
3. Affliction of the soft skeleton
4. Combined

III. Neural form (neurobrucellosis):

1. Affliction of the peripheral nervous system
2. Affliction of the central nervous system
3. Psychobrucellosis

IV. Urogenital form

V. Clinically combined forms

VI. Chronic mixed brucellosis with the concretions in parentheses, for example: brucellosis/malaria, brucellosis/tuberculosis, brucellosis/syphilis.

Note: In addition, the condition of decompensation, subcompensation or compensation is indicated in parentheses.

Many different means and methods have been proposed for the treatment of brucellosis. This circumstance, at first glance, might give some basis to assume that contemporary medicine has no effective agents for combatting brucellosis. Meanwhile, thanks to the efforts of many investigators (P. F. Zdrovovskiy, B. P. Pervushin, G. A. Pandikov, N. I. Ragosa, G. P. Rudnev, A. F. Bilibin, O. D. Sokolova-Ponomareva et al.), our native science has achieved important successes in the treatment of brucellosis. Therefore, it follows to categorically object to false impressions, which still exist in some places, about the incurability of brucellosis patients.

It should be emphasized, however, that there is no single method for the treatment of brucellosis. Many methods are used, particularly:

1. Immunobiological (vaccinotherapy, serotherapy)
2. Chemotherapeutic - sulfonamide (sulfidine, sulfazole, sulfadiazine, etc.), arsenic preparations (neocarsphenamine, sulfarsphenamine, etc.)
3. Antibiotics [synthomycin, levomycetin (chloromycetin), bioxylin (aureomycin), terramycin, streptomycin, tetracycline, etc.]
4. Restoration of the physiological and compensatory mechanisms of the macroorganism (autohemotherapy, roentgenotherapy, tissue therapy by the Filatov method, etc.)
5. Physiotherapeutic
6. General strengthening and symptomatic.

Experiments of Soviet investigators' show that complex treatment has proved to be the most effective in brucellosis.

The value of complex measures in brucellosis is established, first of all, by the complexity of the pathogenesis of this illness, and also by the chronic and multiphased course of the disease, with which occurs a diversity of both functional and organic disorders.

With the conduct of a complex treatment we have in mind:

1. Suppression of the vital activity of the brucella and the elimination of intoxication.
2. Reduction of the excessively increased sensitivity of the organism.
3. Increase of the reactive ability of the organism.
4. Restoration of the physiological and compensatory mechanisms.

In the treatment of brucellosis, by analogy with the treatment of other illnesses, it is necessary to keep in mind the importance of each measure in the individual illness form and also the consequence of their use. This is why, in the future, after some preliminary general notes, we will refer individually to the treatments of acute, subacute, and chronic forms of brucellosis. In prescribing a certain method of treatment for a patient it is necessary to strictly observe the principle of the individual approach, i.e., to treat not the disease but the patient as an individual complete organism.

It is well known that the condition of the patient's nervous system has a great influence on the course and outcome of every illness. Daily clinical experience teaches that a depressed mood, nervous-psychic trauma, etc., cause a more protracted and more difficult course of the disease. Therefore it is extremely important to use all possible measures for normalization of the nervous activity by instilling confidence in the patient as to the favorable outcome of the disease by means of removing the various factors that exert an unfavorable influence on the patient's psyche. Together with this it is often expedient to use bromide preparations, which, according to the observations of N. K. Petrova, exert a regulating influence on the nervous activity by eliminating nervous-psychic dysfunctions.

Prolonged physiological sleep and a diet that is full value in regards to quantity and quality, with a sufficient vitamin content, particularly vitamin C, are important treatment factors in a system of therapeutic measures for a brucellosis patient.

In addition to the basic method of treatment there is a symptomatic therapy that is widely used, as dictated by the indications; with this are prescribed the general strengthening preparations - cardiac stimulants and pain relievers, etc.

The best results can be achieved when treatment is started in the earliest period of the disease.

Vaccinotherapy occupies a special place among the therapeutic measures that are useful for brucellosis in general and for its acute and subacute forms in particular.

In an official instruction that was issued by the Scientific Medical Council and the Main Sanitary-Antiepidemic Administration of the Ministry of Public Health of the USSR, dated 24 March 1953, and developed by G. P. Rudnev, A. F. Bilibin and N. D. Beklemishev, it is recommended to use vaccine in the chronic as well as in the acute and subacute forms of brucellosis.

Some investigators (N. I. Ragoza) are against the use of vaccine in the acute period of brucellosis, the principal considerations being that it is difficult to visualize the effect of injecting one million or even 10 million killed brucella microorganisms when the organism is inundated with live brucella in such number that they will exceed the killed brucella a thousand times.

However, the observations of many authors (G. A. Pandikov, Ye. P. Chasovnikova et al.) and our materials show that a positive result is observed with vaccination in acute and subacute cases of brucellosis. On the other hand, at present, the direct effect achieved by antibiotics in acute and subacute brucellosis is more regular and quicker than in the treatment with vaccine. Therefore, the early use of vaccine for brucellosis patients at the present time is objected to.

The data in the literature and our own observations enable us to give the following antibiotics first preference in the treatment of brucellosis, particularly in the acute and subacute periods and also in the exacerbations of chronic brucellosis with a fever: synthomycin, levomycetin, bioamycin and streptomycin. The prescription of the indicated antibiotics, as a rule, leads to a drop of the temperature to normal, a lessening of the toxemia, improvement of the general condition, reduction in the size of the liver and spleen, etc. With this the best results are received with the cyclic treatment of brucellosis (I. L. Bogdanov).

The plan of treatment with levomycetin: the first cycle - 0.5 gram 6 times per day for 7-8 days, a total of 21-24 grams, then a break of 5-7 days; the second cycle - 0.5 gram 6 times per day for 6 days, a total of 18 grams, then a break of 6 days; the third cycle - 0.5 gram 4 times per day for 4-6 days, a total of 8-12 grams. The total amount of the preparation is 47-54 grams. The same method can be recommended for treatment with synthomycin.

Bioamycin (aureomycin) is given internally 6 times per day. A single dose comprises 200,000 units, a daily dose is 1,200,000 units. The continuance of treatment is 7-10 days. After 10 days it is expedient to repeat the course of treatment; the continuance of the repeat course is 5 days (6,000,000 units).

Observations about the use of streptomycin are relatively rare. The majority of investigators indicate the undoubted efficacy of this preparation (T. Kh. Madzhiddinov, N. D. Beklemishev et al.), particularly in combination with sulfonamide preparations.

Streptomycin is prescribed 0.5 gram per day, intramuscularly, a total of 20-30 grams for the course. Together with this it should be pointed out that experimental investigations, particularly the observations of G. A. Balandin and N. P. Prostetova, show that streptomycin exerts neither a sterilizing nor inhibiting effect on the development and course of a generalized experimental brucellosis infection in white mice and guinea pigs.

During recent times a polyantibiotic therapy of brucellosis has been recommended, i.e., a parallel prescription of two antibiotics, for example, streptomycin / synthomycin, synthomycin (levomycetin) / bioamycin, and in cases that persistently fail to respond to treatment, three antibiotics are used - synthomycin or levomycetin / streptomycin / bioamycin.

There are indications in the literature about a toxic effect of some antibiotics on the liver. In a study, which was made by means of aspirational biopsy, of the morphological changes in the human liver prior to, during and after treatment with aureomycin (bioamycin), terramycin and chloromycetin (levomycetin), they detected a fatty infiltration and vacuolation of the hepatic cells; these manifestations receded within 5 days after cessation of treatment. Together with this there were also noted clinical indications of avitaminosis. Because of the negative effect of antibiotics in some cases it is recommended that with their prolonged use, one should simultaneously prescribe liver extract or campolon to be taken internally and also vitamin B₁₂ to be given subcutaneously.

Sulfonamides can be prescribed together with antibiotics (streptomycin), or separately, in the acute and subacute forms of brucellosis. These sulfonamides are as follows: norsulfazol, sulfathiazole, phthalazole, sulfidine, etc. The sulfonamides are prescribed to be taken internally in an amount of 40-50 grams for the course.

Prescription plan. First day, 6-8 grams (1 gram every 4 hours); second day, 5 grams; third day, 5 grams; fourth and fifth day, 4 grams; 3 grams per day in the following days.

The sulfonamide preparations are usually prescribed as a temporary form of therapy, after which there are other therapeutic measures used, particularly vaccinotherapy.

Which antibiotic should be given preference? G. P. Rudnev, in touching upon this question, prefers bioycin. I. L. Bogdanov prefers levomycetin. F. D. Madzhaidinov - synthomycin. N. D. Beklemishev - bioycin.

The data in the literature and the experience of our clinic show without doubt that the indicated antibiotics - each separately (monoc antibiotic therapy) or in combination (polyantibiotic therapy) - do not prevent development of the relapses, which occur in 50-70 % of the cases.

Because the introduction of antibiotics into medical practice has not resolved the problem of treating brucellosis, vaccinotherapy should be conducted in conjunction with the use of antibiotics in brucellosis patients.

Vaccinotherapy has received extremely wide acceptance. However, some facets of this method are obscure. To date there is no generally accepted method of administering the vaccine or of its dosage. Also, the mechanism of vaccinotherapy's action is controversial.

The vaccine is administered by various routes: 1) subcutaneously; 2) intracutaneously; 3) intramuscularly; 4) intravenously; 5) combined. In the subcutaneous method the vaccine is injected in the region of the hip or into the subcapularis muscle in increasing doses with each injection.

1st injection	10 million microbic bodies
2nd "	20 " " "
3rd "	40 " " "
4th "	80 " " "
5th "	150 " " "
6th "	250 " " "
7th "	400 " " "
8th "	600 " " "
9th "	900 " " "
10th "	1 billion 300 million microbic bodies.

In the intracutaneous application (Alicov's method), the vaccine is injected in doses from 5-10 to 500 million microbic bodies (most frequently

80 million); with this there is no more than 0.1 cm³ of vaccine injected at a single point of injection and the number of injection points is increased step by step, 0.2 cm³ with 2 points, 0.3 cm³ with 3 points, etc., within 3-4 days.

A repeat course of the treatment is recommended within 2-3 months.

The plan of treatment by the Alisov method is as follows: (see table).

The observations made by our clinic (N. S. Chernokalov) in regards to this method showed that the intracutaneous injections of the vaccine have an advantage in that they do not produce a general reaction and may be widely utilized in those cases where the intravenous and subcutaneous injections of the vaccine are contraindicated.

With the intramuscular method the vaccine is injected into the gluteus or deltoid muscles in the following dosages:

1st injection	100 million microbic bodies
2nd "	200 " " "
3rd "	300 " " "
4th "	500 " " "
5th "	1 billion microbic bodies
6th "	2 " " "

In persistent cases the number of injections may be increased to 10.

The majority of investigators consider that the best method giving the most pronounced positive effect is the intravenous injection of vaccine.

In order to determine the degree of the patient's sensitivity to the vaccine, there are at first 1-2 million microbic bodies injected; subsequently there are 5 million, 10 million, 15 million, 25 million, 50 million, 75 million and 100 million microbic bodies injected. The total number of injections comprise 10-15. The intervals between are 3-5-7 days.

After the intravenous injection of the brucellosis vaccine, usually within 4-5 hours, there is a violent reaction that is accompanied by chill, rise in temperature (to 39-40°C), general indisposition, headache, nausea, sometimes vomiting, aggravation by painful symptoms, focal soreness, and drop in blood pressure (shock reaction). This "postvaccinal" period continues for a course of several hours and sometimes a day. The temperature most frequently drops critically, but the painful sensations and the manifestations of adynamia remain for 1-2 days.

The next injection of the vaccine is made within 1-2-3 days after the abatement of the reaction; if the latter was sharply expressed then the dose should not be increased.

Considering the strong reaction that can be caused by the intravenous injection of vaccine, G. P. Kudnev has proposed a two-stage method of intravenous vaccinothrapy. The first "adjusting" dose of vaccine is recommended

to be injected intravenously in a physiological solution in a quantity of 500 thousand microbic bodies; in weakened patients - 300 thousand - 200 thousand - and even 100 thousand; within 1½-2 hours the second "working" dose of the vaccine is injected in the same amount as in the first. At the extreme, the second dose can be increased 2-3 times and more, depending on the general reaction.

The Rodney therapeutic plan with vaccine:

For 1 infusion	"A" $\frac{100,000}{100,000}$	"B" $\frac{200,000}{200,000}$	microbic bodies
2	$\frac{150,000}{150,000}$	$\frac{300,000}{300,000}$	
3	$\frac{200,000}{200,000}$	$\frac{500,000}{500,000}$	and so forth

Note: "A" refers to the recent cases
 "B" refers to the more prolonged and persistent cases,
 usually with a weaker reaction.

According to the observations of I. L. Bogdanov and V. A. Protsenko, an injection of a 5-10 million vaccine in a ¼% - ½% solution of novocaine will significantly moderate the postvaccine fever and can be used particularly in those cases where a violent temperature reaction is noted for even an insignificant dose of vaccine.

Which method of vaccinotherapy should be given preference?

The materials in the literature and our observations prove that the relapses occur in any method of vaccine injection.

Comparative data, based on material from our clinic, indicate that the routes of administering the vaccine have no particular significance in regards to efficacy when a calculation is made of the end results. Vaccinotherapy is indicated in the acute and subacute forms of brucellosis after therapy with antibiotics.

It should be pointed out that the method of intracutaneous therapy, according to our material, has an advantage over the others in regards to the mildness of its effect on the organism of the brucellosis patient.

In cases of the chronic course of brucellosis, the vaccine can be used in the period of subcompensation and decompensation.

We will analyze the viewpoint held by I. L. Bogdanov, according to which the prescription of vaccine in the compensated chronic forms of brucellosis is impractical inasmuch as this can lead to an aggravation of the infection. Treatment with vaccine is contraindicated when there are expressed changes on the part of the cardiovascular system (endocarditis) or active tuberculosis of the lungs. The vaccinotherapy should be conducted with care in the presence

of deep changes on the part of the kidneys and liver; in such cases it is expedient to combine the vaccinotherapy with the prescription of glucose and vitamins of the B and C groups.

In the treatment of the chronic forms of brucellosis the scope of therapeutic measures are broader. It is proper to prescribe antibiotics during the exacerbation of the process, particularly when there is a febrile condition. After antibiotic therapy it is recommended to use one of the types of vaccinotherapy.

With this it is expedient to use the vaccine intracutaneously under ambulatory conditions and to use it intravenously (by the Rudnev method) or intracutaneously under hospital conditions. The latter is the method of choice in those cases where there are absolute contraindications to intravenous vaccinotherapy (advanced age, nutritional breakdown, deep changes on the part of the cardiovascular system of the liver, etc.).

In these cases it is possible to use antibrucellosis serum prepared by Uvarov's method.

The plan of treatment with Uvarov's serum is:

1st injection	0.6-0.5	cm ³	of serum
2nd "	0.7-0.8	"	" "
3rd "	1.0	"	" "
4th "	1.0	"	" "
5th "	1.0	"	" "
6th "	1.25	"	" "
7th "	1.5	"	" "

The best therapeutic effect is observed with 2-3 courses of treatment with Uvarov's serum in conjunction with the other methods.

In the treatment of unresponsive forms of chronic brucellosis it is useful to prescribe remedies that stimulate the immunogenic activity of the organism and increase its general reactivity; among these are:

1. Blood transfusions (5-7 transfusions for the course);
2. Transfusion of the erythrocytic mass;
3. Tissue therapy by the Filatov method;
4. Autochemotherapy.

The indicated methods can be used either separately or as auxiliaries.

In cases of chronic brucellosis accompanied by a painful sympson complex, which is observed with an affliction of the nervous system (radiculitis, neuritis) and the support-motor apparatus, a novocaine block by the Vishnevskiy method gives good results (injection of 50-100 cm³ of a $\frac{1}{2}\%$ solution into the perinephric cellular tissue). In radiculitis, ischialgia, lumbago, etc., a favorable effect is often produced by the injection of a $\frac{1}{2}\%$ solution of novocaine (total dose is 20-40 cm³) where the pain is most

intense. In some cases at our clinic a daily intravenous injection of 5-10 cm³ of a 1-2% solution of novocaine (for a period of 7-10 days) has been used successfully with diffuse pains.

Physiotherapeutic methods are used extensively in chronic cases of brucellosis with afflictions of the support-motor apparatus and the nervous system. Among these are: 1) light treatment; 2) paraffin therapy; 3) diathermy; 4) ultra-high frequency; 5) iontophoresis; 6) therapeutic gymnastics; 7) roentganotherapy; 8) hydrotherapy, etc.

The observations of A. A. Mokrinskaya and V. M. Klimantova have shown that in the chronic forms of brucellosis, in cases of affliction of the locomotive apparatus, the most pronounced effect was received from the combined use of vaccinotherapy and physical therapy methods (diathermy, paraffin, etc.).

Warm baths (36-37°C), lasting 10-15 minutes, show a favorable effect with brucellosis.

An important place in the complex of therapeutic measures for brucellosis patients is held by resort therapy, in which many factors exert a favorable effect on the human organism (proper regime, climate, balneologic procedures, etc.).

Active resort therapy (mud, salt-water, hydrogen sulfide and radon baths, etc.) can be used for brucellosis patients in the presence of focal afflictions in the compensation stage and also for patients with postbrucellosis afflictions. It is possible to send to a resort those patients whose febrile periods have been ended for not less than 3 months. Those forms having an accelerated rate of erythrocytic precipitation, or a positive Wright reaction - in a range of 1:400 or higher, are contraindicated for use of pelotherapy.

The basic indications for resort treatment, in accordance with the manual, are:

a. For the mud resorts, the chronic forms of brucellosis with afflictions of the locomotive apparatus (chronic illnesses of the joints, muscles, and the peripheral nervous system).

b. For the balneologic resorts with, principally, the radon and sulfide mineral waters (Belokurikha, Tskhaltubo, Sergievskiy mineral waters, etc.), the same forms of brucellosis that are in par. 'a.', but also those having cardiovascular changes in the compensation stage.

The most appropriate resorts for treatment of brucellosis patients are considered to be as follows: Karachi, Medvezh'e, Gor'koe, Uchum, Tagarskoe, Pyatigorsk, Sergievskiy mineral waters, Saratovsk, Lipetsk, Sochi, Tskhaltubo, Muzaldy, and others.

Good results were received in Omsk Oblast in the treatment of brucellosis with the mud from Lake U'dzhay at the Gherlakskiy Rayon Hospital where patients from Omsk and other Rayons of our Oblast are sent in the summer period.

With the complex method of treating brucellosis patients, it is possible to achieve complete recovery when there is timely and rational use of the above-cited powerful preparations and the other methods shown in the attached plan.

Attached hereto you will find a plan for the treatment of brucellosis that is compiled on the basis of the data in the literature (see the plans of G. P. Rudnev, A. F. Bilibin, N. D. Beklemishev, I. L. Bogdanov, T. Kh. Madzhiddinov) and the observations of the facultative therapeutical clinic on the base of the Omsk Oblast Clinical Hospital.

Alisov's Treatment Plan

	Day of treatment												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Amount of vaccine to be injected in the skin of the rt. forearm, in cm ³	0.1	0.2	0.3	0.4	0.5	0.5	0.5	0.5	0.4	0.3	0.2	0.1	4
Number of injection points	1	2	3	4	5	5	5	5	4	3	2	1	40
Amount of vaccine to be injected in the skin of the left forearm, in cm ³	0.1	0.2	0.3	0.4	0.5	0.5	0.5	0.5	0.4	0.3	0.2	0.1	4
Number of injection points	1	2	3	4	5	5	5	5	4	3	2	1	40
Total of microbic bodies, in millions	2	4	6	8	10	10	10	10	8	6	4	2	80

Plan of Treatment For Brucellosis Patients

Type of treatment	<u>Clinical Forms of Brucellosis</u>			
	Acute	Subacute	Chronic in the phase of exacer- bation	Residual manifesta- tions
Anti biotic Therapy (mono or polyantibiotic therapy):				
a. Bionycin	Yes	Yes	Yes	No
b. Levomysetin	Yes	Yes	Yes	No
c. Synthomycin	Yes	Yes	Yes	No
d. Terramycin *	Yes	Yes	Yes	No
e. Streptomycin	Yes	Yes	Yes	No
f. Penicillin	Yes, with secondary infec- tions, that is.			No
Vaccinotherapy				
a. Intravenous (by Galelmo's method)	No*	No*	Yes	No
b. Intravenous (by Radnev's method)	No*	No*	Yes	No
c. Intracutaneously (by Alisov's method)	No*	No*	Yes	No
d. Subcutaneously, intra- muscularly (by the method of Hagood and Panikov's)	No*	No*	Yes	No
Chemical Therapy (Sulfanilamide preparations)				
	Yes**	Yes**	In indi- vidual cases	No
Transfusion of blood and other types of stimulant therapy (tissue therapy, Starov's serum, etc.)				
	No	In indi- vidual cases.	Yes	Yes
Hematogenotherapy				
	No	No	Yes	Yes
Physiotherapy (quartz, paraffin, salt, etc.)				
	No	In indi- vidual cases.	Yes	Yes
Resort Treatment				
	No	No	Yes***	Yes***
Symptomatic Treatment (general strengthening, cardiac, sedative, analgesic, etc.)				
	Yes	Yes	Yes	Yes
Vitamin therapy				
	Yes	Yes	Yes	Yes

* In the acute and subacute forms of brucellosis it is best to conduct the
vaccinotherapy after antibiotic therapy.

** Best in conjunction with streptomycin.

*** Indicated with focal afflictions where there has been no fever for no less
than 3 months.