

cases that the polymorphonuclears numbered from 65 to 70 per cent., the large mononuclears from 7 to 10 per cent., the small mononuclears from 17 to 21 per cent., transitional forms from 1 to 3 per cent., eosinophils from 2 to 4.5 per cent. Biffi⁸ found the polymorphonuclears 44 per cent., eosinophils 10 per cent., large mononuclears 16 per cent., lymphocytes 30 per cent. In the severest case which we encountered, the polymorphonuclear leukocytes numbered 56 per cent., the large mononuclears 16 per cent., transitional forms 0.1 per cent., small mononuclears 12 per cent., eosinophils 0 per cent., normoblasts 9 per cent., myelocytes 2.5 per cent. Myelocytes are found present in the severe cases ranging usually from 0.5 to 2 per cent. The hemoglobin in severe infections may amount to but 15 per cent. In less severe cases of infection it may be from 40 to 50 per cent. In our first publication we gave a description of the parasite as it occurred in the red blood-cells. Other forms of it have subsequently been found in the endothelial cells. To this parasite, which we believe causes the disease, we have given the name of *Bartonella bacilliformis*.⁹ In another report which will shortly appear, this organism is fully described, and the description of its life cycle in the endothelial cells considered. In severe cases, the parasites which give rise to the disease are present in the red cells in great numbers. In mild cases, however, the number of infected corpuscles is small and a long search is often necessary to disclose the parasites.

CLINICAL EXPERIENCE WITH LIQUID PARAFFIN (LIQUID PETROLATUM)

A COMPARATIVE INVESTIGATION MADE UNDER THE AUSPICES OF THE COUNCIL ON PHARMACY AND CHEMISTRY *

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During the past three or four years, "mineral oil" has come into extensive use in the treatment of constipation. Preparations of the Russian and the American oil, both heavy and light, have appeared on the market, but there have been no satisfactory data on which to base a selection of oil for use. Therefore, in order to obtain reliable clinical information concerning the relative efficiency of the different oils, the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association submitted samples of the oils to various clinicians for testing. The following is a synopsis of the investigation, which I have prepared at the request of the committee.

The collaborators were advised that specimens of the best obtainable light Russian liquid petrolatum, heavy Russian liquid petrolatum and an American brand of

liquid petrolatum would be sent out, but that, to avoid bias, these specimens would be distinguished only by numbers or letters. The oils sent out were (1) a light "Russian" liquid petrolatum having a specific gravity of 0.860 at 20 C., (2) a heavy "Russian" liquid petrolatum having a specific gravity of 0.885 at 20 C., and (3) an "American" liquid petrolatum having a specific gravity of 0.857 at 20 C. and being markedly fluorescent. The collaborators were advised that the reports should furnish information as to size and frequency of dose, the agreeableness to the taste, the effect on the stomach, the number and character of the stools, the degree of admixture of the oil with the other ingredients of the stool, the degree of leakage of oil about the anus, and the need of other cathartic measures.

Reports have been received from Drs. L. F. Barker, W. A. Bastedo, J. B. Champion, Henry A. Christian with C. K. Drinker and F. A. Hatch, Alfred Stengel and R. L. Wilbur.

CONCLUSIONS

The conclusions to be drawn from the clinical reports are:

Dosage.—Half an ounce to 3 ounces a day. In the same patient, the same amount of each of the oils was required.

Frequency of Dose.—The same amount daily seemed as efficient when given in one dose as when given in divided doses two or three times a day.

Agreeableness to the Taste.—There is a difference of opinion in this regard. Two reports favored the heavy Russian oil. One report favored the light Russian petrolatum. But the taste of any of the samples was so slight as to be a negligible quantity after the patient had taken the remedy for two or three days.

Stomach Effects.—In about 20 per cent. of the patients, the oil produced a slight degree of nausea or tended to repeat. This is most likely in patients who have gastric stagnation with retarded emptying of the stomach. All the oils acted the same in this regard. Vomiting was reported in two cases.

Number of Stools.—To produce one or two copious stools a day the dose required varied considerably, but there was no difference noted on account of difference in the specific gravity or character of the oils.

Character of Stools.—The stools were soft, usually formed, sometimes mushy, obviously greasy. They had a peculiar odor described as sour. Their consistency varied with the dose, but was the same for the different kinds of oil.

Admixture of Oil with Other Ingredients of Stool.—Generally well mixed, but from time to time a patient would have a stool of free oil. This occurred with all varieties of oil. (It necessitated reduction of the dose, and if then the bowels were not active enough, the administration in addition of cascara, aloin, etc.)

Leakage About the Anus.—A disagreeable feature complained of by many is that when they take enough of the oil to move the bowels, there is sufficient leakage from the anus to keep the neighboring skin continually in a greasy condition, and sometimes to stain the clothes. That there is any difference in this regard between the oils has not been determined.

In the reports, one clinician noted no differences that were not negligible. Another was slightly in favor of No. 2 (heavy Russian) as regards taste. A third reporter did not make comparative tests. A fourth is

8. Biffi: Bol. Acad. de med. de Lima, 1903, iii, 2.

9. Dr. P. W. Bassett-Smith has since our first publication in THE JOURNAL kindly called the attention of one of us to the fact that the name *Bartonia* first suggested by us, has been used as a generic one in botany to include two species of Gentianaceae. This use would not necessarily preclude its employment in zoology, although a duplication of names in botany and zoology is certainly highly undesirable. On investigation, however, we have found that the use of *Bartonia* as a generic name has been applied by Cossmann (Paris, 1901, p. 293) to an eocene mollusk, *Bartonia canaliculatum*; hence we have changed the generic name to *Bartonella*, retaining the specific one, *bacilliformis* (*Bartonella bacilliformis*).

* This investigation was made under the auspices of the Committee on Therapeutic Research of the Council on Pharmacy and Chemistry of the American Medical Association. At the request of the committee, Dr. W. A. Bastedo has prepared this critical review of the reports made by those who collaborated in this investigation.

slightly in favor of "B" (heavy Russian) as regards taste and general suitability. All of the findings of this investigation are based on hospital cases. A fifth reporter favored No. 1 (light Russian petrolatum). He considered it the most prompt in its effect, the most uniform in results, and the most prone to give a satisfactory admixture of the oil with the other materials. The difference, however, from the other oils was not marked. Another reporter noted no special differences.

SUMMARY

The results of this clinical investigation appear to warrant the conclusion that so far as therapeutic results are concerned the differences in the action of the three varieties of liquid petrolatum, namely, light Russian liquid petrolatum, heavy Russian liquid petrolatum and American liquid petrolatum, are too slight to be of importance. Hence the choice between the lighter and the heavier oils, and between the Russian and the American is an open one, to be determined not by therapeutic differences, but by palatability, dependent on the degree to which the refinement of the oil is carried out. The U. S. Pharmacopeia, the revision of which is now nearing completion, no doubt will furnish standards which will insure a suitable product. From the findings of the foregoing report it would appear that a satisfactory standard might permit the use of either Russian or American oil, if suitably refined so as to be as nearly as possible devoid of odor and taste.

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A STUDY OF THE COMMERCIAL PREPARATIONS OF BACILLUS BULGARICUS

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During the past few years many physicians have advocated the administration of living cultures of *Bacillus bulgaricus*, in order to change beneficially the intestinal flora. It is asserted that the large amount of acid produced by this organism from the fermentation of the various sugars is detrimental to the growth of other intestinal organisms, especially of the putrefactive group. This organism was at first given in the form of a fermented milk, but is now dispensed chiefly in the form of pure cultures, either in liquid or in tablet form. The potency of these cultures was the object of this investigation.

These cultures are sold either as liquid cultures—broth or whey—or in the dried form as tablets. The majority of the manufacturers simply label their product as living cultures of *Bacillus bulgaricus*, but do not state how many living organisms are present. Some state the number of bacilli present, but add that the count was made by some staining method (Wright), which method does not differentiate between living and dead organisms. As the therapeutic agent is the acid produced by the metabolism of the living organism, any count which does not differentiate between living and dead organisms is of no importance.

The *Bacillus bulgaricus* grows with difficulty on the usual laboratory mediums, but grows readily on mediums containing milk or whey. It ferments glucose and lactose readily, producing a large amount of acid, and the resulting acidity gradually kills the organism. It is this factor of acid production which

is one of the principal causes of the rapid deterioration of the liquid preparations.

The names of the preparations tested are not given because not sufficient of each was tested to say which were uniformly bad or good. In the liquid preparations, those giving the highest counts were all obtained direct from local manufacturers from freshly prepared lots. The same preparations bought in the open market in other parts of the country would undoubtedly show much poorer results. In the more complete investigation which is being continued, I hope that results will be more definite, and that I shall be able to publish the names of those manufacturers who control their product so that it is uniformly good, and also to expose those whose preparations are practically inert or heavily contaminated.

In order to make an exact count of the number of living organisms in the preparation, it is necessary to plate them in suitable mediums in varying dilution, and after incubation to count the number of colonies. As the different strains of *Bacillus bulgaricus* vary in their cultural characteristics, each specimen was plated on four different mediums, and the highest count obtained on any one of the four mediums is the count that is listed. Plates were examined after three days' incubation at 40 C. (104 F.). The final count was made after five days' incubation.

The following plating mediums were used.

1. Veal infusion glucose agar.

To the veal infusion were added 2 per cent. agar, 2 per cent. glucose, 0.5 per cent. salt and 2 per cent. peptone, and the medium was titrated to 1 per cent. acid to phenolphthalein.

2. Whey glucose agar.¹

Whey was obtained by adding glacial acetic acid to hot milk. To this were added 2 per cent. peptone, 2 per cent. agar and 1 per cent. glucose, and titrated to 1 per cent. acid.

3. Whey glucose calcium carbonate agar.²

This was the same as the previous medium, with the addition of a few drops of sterile powdered calcium carbonate in water just before plating.

4. Veal infusion whey glucose agar.

This was the same as the first medium, but after cooling to 45 C. (113 F.), one-fourth the volume of warm whey was added. This whey was prepared by rennet coagulation of certified milk. The coagulated milk was heated in the Arnold, and the whey thus obtained was filtered through paper and then sterilized.

Each specimen was also inoculated into the following tube mediums:

1. Litmus milk.
2. Whey.
3. Peptone glucose whey.
4. Veal infusion broth.

These tube inoculations served to control the plating mediums. In no case in which similar organisms were not obtained on one of the plating mediums was a growth obtained in any of the tubes.

The following specimens were tested:

1. Liquid. Obtained direct from manufacturer, freshly prepared lot. Broth culture in small bottles. Not dated.

1. Heineman and Hefferan: A Study of *Bacillus Bulgaricus*, Jour. Infect. Dis., 1909, vi, 304.

2. Bendick: The Use of Calcium Carbonate in Solid Media for the Differentiation of Sugars Fermenting Bacteria, THE JOURNAL A. M. A., Oct. 21, 1911, p. 1343.