BACTERIAL INVASION OF BLOOD AND CEREBROSPINAL FLUID BY WAY OF LYMPH-NODES

FINDINGS IN LYMPH-NODES DRAINING THE PELVIS *

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The present communication is the fourth of a series dealing with a possible path of meningeal infection. The previous (or third) and second communications dealt with the bacterial invasion of the blood and cerebrospinal fluid in the light of findings, respectively, in the bronchial (fifty cases) and the retroperitoneal (thirty cases) lymph-nodes, and in the mesenteric (fifty cases) lymph-nodes. The second (or mesenteric lymph-nodes) communication developed an idea based on a previous paper by Gay and Southard¹ on the general significance of bacteria cultivated from the cadaver.

Our efforts have been directed at throwing light (so far as routine necropsy cultures might) on the curious fact observed by Gay and Southard that, whereas 41 per cent. of the bloods remained sterile with the methods used, on the other hand only 28 per cent. of the cerebrospinal fluids remained sterile.

Concerning the general problem we shall say no more than that the blood percentages obtained by Gay and Southard with insane hospital material compare well with those of other workers (mentioned in previous communications) with general hospital material, that our work has not necessarily anything to do with the general controversy between the "intravitalists" and the "postmortalists" as to the meaning of bacteria grown from the cadaver, and that there are no available data from other workers concerning our high positive percentages in the cerebrospinal fluid. The cerebrospinal fluid has been shown by Gay, and independently by McKenzie and Martin, normally to contain no bacteriolytic substances, whereas the blood is well known to contain such both in life and for some time after death.¹

We were led to the obvious idea that bacteria from whatever source—infected lesion or some surface drained by lymph-nodes—might enter the blood, infect the meninges, die out in the blood, and persist in the cerebrospinal fluid. (Of course, it is also conceivable that organisms may in some way enter the cerebrospinal sheath from lymph-vessels without passing through the blood: the solution of the latter problem can hardly be by such statistical work as we now report.)

In point of fact, our cultivations from three loci (mesenteric lymph-node, blood and cerebrospinal fluid) gave the expected result that the most frequent positives in two out of three loci occurred precisely in the lymph-node-fluid combination. Fortunately for certain pur-

poses, though unfortunately for others, our mesenteric gave positive results (with one or more organisms) from lymph-node comparative cultivations were made during a dysentery epidemic, which so enriched the flora with secondary invaders that actually 55 per cent. of the cases all three chosen loci² (mesenteric lymph-node, blood and cerebrospinal fluid).

We went on to study in similar comparative fashion the organisms cultivable from bronchial lymph-nodes, blood and cerebrospinal fluid.³ The fluid persisted in leading both blood and lymph-nodes in percentages of positive cultivations. But, although the bronchial lymph-nodes led the blood in positives, yet the combination of positives in lymph-node and fluid was decidedly uncommon in this bronchial node investigation. Also only 35 per cent. of the cases yielded positives in all three loci (bronchial lymph-node, blood and cerebrospinal fluid). Accordingly we suspected that the bronchial lymph-nodes had somehow less to do with invasion of the cerebrospinal sheath than the mesenteric lymph-nodes.

We then resorted to cultivations from retroperitoneal lymph-nodes⁴ against the other loci. In the latter small series (thirty cases) we actually found the lymph-nodes leading the cerebrospinal fluid as well as the blood in point of positives. Moreover, we found the retroperitoneal series resembling the mesenteric series in the preference among binary positive combinations displayed by the lymph-node-fluid combination.

The mesenteric lymph-node results, as hinted before, may have been essentially modified by the epidemic conditions in the summer of 1909 at the Danvers hospital. We felt that an investigation narrowed to lymph-nodes draining the pelvis would offer us special correlations with particular lesions and germ-bearing surfaces. Instead of general hospital conditions tending to swell and infect the mesenteric lymph-nodes, we should study special conditions tending to produce localized invasions.

Here perhaps it may be observed that we are taking sides rather with the intravitalist than with the postmortalist in respect to these invasions of various parts of the body by bacteria.

The results in our twenty-eight pelvic lymph-node cases are given in Table 1.

TABLE 1.—PELVIC LYMPH-NODE SERIES

Hrs. post mortem	No. of Cases	Percentages		
		Heart's Blood	Cereb. Fl.	P. L.-N.
0-2	1	0	0	100
2-4	0	0	0	0
4-6	2	100	50	50
6-12	7	85	42.5	85
12-24	13	61.5	76.9	69
24-48	2	100	50	100
48+	3	33	66	66

Fusing results in pelvic with those in retroperitoneal lymph-nodes the results are as given in Table 2.

TABLE 2.—PELVIC AND RETROPERITONEAL LYMPH-NODES

Hrs. post mortem	No. of cases	Percentages		
		Heart's Blood	Cereb. Fl.	L.-N.
0-2	2	0	0	100
2-4	0	0	0	0
4-6	4	75	75	75
6-12	14	93	71	93
12-24	22	68	86	77
24-48	4	75	50	100
48+	5	40	60	60

* From the Laboratory of the Danvers State Hospital, being Danvers State Hospital Contributions No. 42, 1913, and a sequel to the same Contributions Nos. 18 and 8. This work has been aided by the Investigation Fund of the Massachusetts Board of Insanity and the Underhill Fund for Neurological Investigation, Harvard Medical School.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Sixty-Fourth Annual Session held at Minneapolis, June, 1913.

1. Gay and Southard: The Significance of Bacteria Cultivated from the Human Cadaver: A Study of 100 Cases of Mental Disease, with Blood and Cerebrospinal Fluid Cultures and Clinical and Histologic Correlations, *Centralbl. f. Bakteriol.*, 1910, iv.

2. Southard and Canavan: Bacterial Invasion of the Blood and the Cerebrospinal Fluid by Way of Mesenteric Lymph-Nodes: a Study of Fifty Cases of Mental Disease, Danvers State Hospital Laboratory Papers, 1910, No. 8, Boston Med. and Surg. Jour., 1910, clxiii.

3. Southard and Canavan: Second Note on Bacterial Invasion of the Blood and the Cerebrospinal Fluid by Way of Lymph-Nodes: Findings in Bronchial and Retroperitoneal Lymph-Nodes, Danvers State Hospital Contributions, No. 18, 1912, Boston Med. and Surg. Jour., 1912, clxvii.

There are perhaps again no significant differences in the flora of these loci as cultivated post mortem. If the invasions are post mortem, the chances favor the hypothesis that the invasions occur early (say in the first few hours) after death.

The kinds of bacteria cultivated are shown in Table 3. As in former work, Chester's "Determinative Bacteriology," 1901, has been largely followed.

TABLE 3.—TWENTY-EIGHT NECROPSIED CASES

	Heart's Blood	Cereb. Sp. Fl.	P. L.-N.
Cocci:			
Streptococci-Micrococci	1	..	..
Albus	..	1	..
Others non-pigmented	3	5	1
Citrus	1	..	..
Others pigmented	2	..	1
Unidentified cocci	..	1	1
Bacteria:			
Hemorrhagic septicaemia	1	2	1
Sanguinarum	..	..	1
Anthrax group:			
Anthraxoides	3	4	2
Rugosum	..	3	..
Truncatum	1	3	1
Subtiliforme	1	1	..
Varicosum	2	..	..
Fermentatilis	..	..	1
Bacilli:			
Coli group	2	..	4
Formosus group	1	..	1
Citrus	..	1	..
Pannicelli	..	..	1
Bassoni	..	1	..
Antenniformis	..	..	1
Strassmanni	1	..	..
Sulphureus	1	..	..
Lesagei	..	..	1

Growths of some sort were obtained from the plates as in Table 4.

TABLE 4.—SOURCE OF GROWTHS

	Cases	Per Cent.
Heart's blood	19 in 28	68
Cerebrospinal fluid	18 in 25	72
Pelvic lymph-node	21 in 28	75
Growths from no region	..	2
Growths from one region and not from the other two:		
Heart's blood	0	0
Cerebrospinal fluid	..	0
Pelvic lymph-node	2	2
Growths from two regions and not from the third:		
Heart's blood and cerebrospinal fluid	3	3
Heart's blood and pelvic lymph-node	3	3
Cerebrospinal fluid and pelvic lymph-node	3	3
Growths from all three regions	10	10

It is interesting to note that these pelvic lymph-nodes, like the higher group of retroperitoneal lymph-nodes studied in the previous communication, are richer in positive cultivations than the cerebrospinal fluid. It is accordingly not unlikely that, as a general rule, the pelvic and retroperitoneal lymph-nodes are more likely to harbor micro-organisms than the mesenteric or the bronchial lymph-nodes.

Like the groups previously studied, the pelvic nodes persist in leading the heart's blood in percentage of positive cultures. This, we assume, is but natural not only because the lymph-nodes are nearer the usual sources of bacteria, but also because in the fluid blood organisms which reach it are readily killed.

No further example (like one in the retroperitoneal series, 1414) of a positive blood with other loci negative was found in the pelvic series.

Since all the binary combinations are equally productive of positive cultivations, no conclusion can be drawn as to preferences for the different loci.

Three cases yielded the same organism in all three loci:

CASE 1.—14079, Path. 1398, man aged 40, general paresis, with purulent prostatitis, showed *Bacterium anthracoides* in pure culture in pelvic (inguinal), mesenteric, bronchial lymph-nodes, in heart's blood and in cerebrospinal fluid.

CASE 2.—15255, Path. 1404, man aged 40, general paresis, with pulmonary tuberculosis, hypertrophied prostate and injected bladder, showed *Bacterium gallinarum* in bladder, pelvic lymph-node, blood and cerebrospinal fluid; *Bacillus formosus* in lymph-node along aorta; *Bacterium anthracoides* and unidentified cocci in pus from right ear, and unidentified cocci in other pelvic and in retroperitoneal lymph-nodes sixteen hours post mortem.

CASE 3.—14779, Path. 1413, male, aged 16, dementia praecox, with injection of prostate and bladder and death from typhoid fever and peritonitis, showed in urethra, pelvic, retroperitoneal and aortic lymph-nodes, heart, cerebrospinal fluid, *Bacterium sanguinarum*, in peritoneal fluid *Bacterium pallidum*, two hours post mortem.

The foregoing three and six other cases showed the same organism in pelvic lymph-nodes and in cerebrospinal fluid (nine cases).

CASE 4.—14656, 1385, woman aged 46, Huntington's chorea, *Bacterium anthracoides*, nine hours post mortem.

CASE 5.—15195, 1390, woman aged 51, organic dementia, cocci, sixteen hours post mortem (cocci also in decubitus).

CASE 6.—15495, 1397, woman aged 59, involution melancholia, *Bacterium anthracoides*, thirty-nine hours post mortem.

CASE 7.—15497, 1402, man aged 36, status epilepticus, *Micrococcus lactis*, twelve hours post mortem.

CASE 8.—12367, 1409, man aged 57, manic-depressive, *Bacterium truncatum*, eighteen hours post mortem.

CASE 9.—15577, 1416, woman aged 68, organic dementia, *Bacterium citreum*, nine hours post mortem.

These findings raise the hypothesis of invasions (whether antemortem or postmortem is here of no account) of two loci often supposed to be closed from one another: a ready hypothesis might be that in the first three cases listed the blood served to spread the bacteria either mechanically or as a growth medium, and that in the last six, the blood, if ever invaded, had killed out its contained bacteria.

In connection with pelvic nodes, it becomes of interest to inquire whether or not acute or chronic pelvic lesions bear any relation to the bacteria cultivated from the nodes. As is not infrequent in insane hospital material, pelvic lesions were numerous. There were in fact but five cases, in which acute or chronic pelvic lesions can be safely excluded according to the necropsy protocols; these five cases yielded sterile pelvic lymph-nodes (1387, 1388, 1406, 1410, 1414), although other lymph-nodes and loci yielded various cultivations.

Of the twenty remaining cases, all but two had pelvic lesions of an acute appearance (four associated with chronic lesions); the remainder (1397 and 1415) have only chronic lesions. Only five of these twenty cases of pelvic lesion failed to show bacteria in pelvic lymph-nodes (1393, prostatic cysts, psoas abscess; 1395, acute cystitis; 1401, rectal injection (lesion?); 1407, acute cystitis (gastric carcinoma); and 1417, injection of bladder. As can be observed, at least three of these cases are to no marked degree diseased as to pelvis, if at all.

As to the general capacity of these loci to receive and care for the larger groups of bacteria (Chester following Migula), we find:

Cocci: in lymph-node 5, cerebrospinal fluid 7, heart's blood 8.

Bacilli: in lymph-node 14, cerebrospinal fluid 10, heart's blood 11.

Bacteria: in lymph-node 4, cerebrospinal fluid 0, heart's blood 3.

SUMMARY AND REMARKS

1. This continuation of our former work shows that the cerebrospinal fluid (72 per cent.) still leads the

heart's blood (68 per cent.) in percentage of positive cultures (routine aerobic methods, post-mortem material).

2. Pelvic lymph-nodes (like mesenteric nodes in our former work) lead both blood and cerebrospinal fluid (75 per cent.).

3. This is possibly due to the great percentage of pelvic lesions in the present series (twenty out of twenty-five cases; fifteen of the twenty showing organisms in pelvic lymph-nodes).

4. It is still uncertain whether these findings indicate ante-mortem or post-mortem invasions. Of course an acute or chronic lesion may conceivably help the penetration of organisms from without.

5. If (as seems likely) the invasions are intravital or agonal, then it would appear that the pelvic lymph-nodes are accustomed to harboring many bacteria (compare the mesenteric lymph-nodes in an epidemic of dysentery²).

6. Whether this habit of receiving more organisms than other nodes induces any superiority on the part of these nodes in respect to their power of digestion, we cannot say. If so, a rationale for Fowler's drainage position (upper part of abdomen maintained higher than lower part), might be imagined. Such a rationale would be superior to saying that the pelvic peritoneum is a better filter than others or is differently constructed from peritoneum elsewhere.

7. The pelvis, often subject to acute and chronic disease in the insane, appears to supply its lymph-nodes with very numerous bacteria (both motile and non-motile and of many groups). Some of these are saprophytes, some doubtless pathogens: they are often found in the cerebrospinal fluid post mortem, even when absent (destroyed?) in the blood. The pelvis compares, under the random conditions studied, with the intestinal tract in its habit of supplying bacteria to regionary lymph-nodes; and perhaps the pelvis surpasses the intestinal tract, since the latter's lymph-nodes happened to be studied during an epidemic of intestinal disease which provided an excess of secondary invaders.

8. The hypothesis of a route of meningeal invasion by way of the blood receives added support from this work, although the possibility of more direct invasion must be considered.

ABSTRACT OF DISCUSSION

DR. H. E. ROBERTSON, Minneapolis: For many years the bacteriology of dead bodies has been the subject of a great deal of discussion, and considerable contempt has been thrown on attempts to isolate pathologic micro-organisms from the body after death and draw any conclusion in regard to their influence on the body before death. There are still some questions which we should like to have Dr. Southard settle for us. Are all kinds of bacteria continually entering the blood from the intestinal tract and continually being taken care of by the protective influences of the blood? This question might perhaps apply not only to the blood, but also to the lymph and the cerebrospinal fluid. What is meant by the agonal invasions of bacteria into the blood and the lymph-nodes? Have we any particular reason to believe that there is any more invasion into the blood and lymph-nodes during abnormal processes than continually during the normal life? Have there been any actual experiments to show whether or not bacteria do pass out into the fluid of the peritoneum, into the blood-vessels or into the lymph-streams after death?

DR. HENRY ALBERT, Iowa City, Iowa: Were examinations of the blood and cerebrospinal fluid made before death in those cases in which they were made at post-mortem? In what proportion of the cases was the dysentery bacillus found in the mesenteric lymph-nodes?

DR. E. E. SOUTHARD, Boston: I had thought from the early work that organisms were continually going through from the intestines into the blood and being continually killed there, and I was somewhat impressed with the work of McDonald concerning the probable infective condition of normal organs during life in most cases. When I found, however, how few cultivable organisms there were in my Boston series I began to wonder whether this was the case. Someone ought to endeavor to make a complete bacteriologic study of the dead body. I do not suppose that anyone has ever done that. Until that is done I do not see how the question of the continual supply of the blood with the bacteria can be settled, but I am of the opinion that it is a continual supply, perhaps from the lymph-nodes, but perhaps more often from the pelvis. Agonal invasions should be less common than non-agonal invasions on account of the well-known immobility of persons who are dead. Experimental work in this department should be done on various parts of the body. In fact, I have been tentatively doing some work in this direction in the pelvis, which I hope I may be able to bring evidence of at a future meeting. An elaborate report of a dysentery epidemic was published in the *Boston Medical and Surgical Journal* in 1910. A rather small number of dysentery bacilli were cultivated in that series. In a certain number of cases comparisons of the blood have been made, but the number is not large enough to warrant any statistical conclusions.

REPORT OF THE COMMITTEE ON THE TREATMENT OF PUERPERAL FEVER *

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At the last meeting of the American Medical Association held at Atlantic City, Dr. T. J. Watkins read a paper on the treatment of puerperal infection, advocating a non-interfering, expectant policy. In the discussion that followed, two widely divergent opinions were voiced. Some would immediately attack the uterus and empty it of its contents; others would wait for Nature to expel ovular remnants.

In proposing that a committee be appointed to investigate the subject, three purposes were kept in mind: (1) to obtain the opinions of authorities and of the profession at large, thus to learn what is the general teaching and practice of to-day; (2) to call general attention to the importance of the subject; (3) if possible, to formulate a course of procedure which would be generally applicable to the treatment of sepsis with retained ovular material.

It was decided to send a letter of inquiry to the profession. The questions reproduced herewith were sent out as follows: 400 letters to professors and assistant professors of obstetrics and gynecology in the United States and Canada; 200 to professors and assistant professors of surgery in the United States; 60 to professors of obstetrics and gynecology abroad—to England, Ireland, Scotland, Germany, France, the Netherlands, Russia and Italy. In addition, the first three questions were published in *THE JOURNAL*.

In all, 302 replies were received, of which 197 came from obstetricians and gynecologists, 53 from surgeons,

* Read in the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.