ON THE CLINICAL BEARING
OF
SOME EXPERIMENTS ON PERITONEAL
INFECTIONS

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Received October 16th, 1896—Read March 9th, 1897.

No doubt much of the *experimental* work which has been done in the past will be utilised *clinically* in the future. Although at present we are unable to apply results derived from the laboratory to the welfare of our patients, yet it is of importance that we should avail ourselves as far as possible of this great means of adding to our powers of diagnosis, and more especially of treatment.

No apology is therefore necessary for calling your attention to the experimental results which I propose to lay before you, since they appear to have a distinct bearing on the treatment of, and on the safeguard from infections of the peritoneum.

The first point to be raised is in regard to a means of prophylaxis in cases where there is some probability, or at any rate some possibility, of unavoidable contamination of the peritoneal cavity if a trans-peritoneal operation is

undertaken (such as abscesses of typhlitic or pyosalpingitic origin).

In 1894 Dr. Issaëff,¹ a bacteriologist, published in Germany a remarkable series of experiments upon peritoneal infections which arose in connection with investigations upon the cholera vibrios.

So far as I am aware, the results of these observations on animals have never been suggested as available for use upon man.

He showed that several different substances, when injected into the peritoneal cavity of guinea-pigs, were capable of affording protection to the animals which were inoculated with cholera vibrios upon the following day. By means of the preliminary injections an increase of the "power of resistance of the part" is established, so that an otherwise fatal dose of microbes can be tolerated; this condition is attained in about twenty-four hours, and lasts about four days. It is to be observed that this condition of exalted general resistance has nothing to do with specific or special immunity; an animal protected by means of a previous injection of simple saline solution is rendered refractory not only to cholera and other vibrios, but also to other pathogenic organisms (*Bacillus typhi abdominalis*, *B. coli*, *B. prodigiosus*, &c.). It also differs in its transient nature; specific immunity gives a more intense and more lasting protection against the specific microbe.

Many writers on immunity have failed to take cognizance of the difference between these conditions of "local general resistance" and "specific immunity," so that often their deductions have to be weighed with caution in regard to the complex question of immunity.

Issaëff's experiments were made with a variety of different kinds of vibrio, after previous treatment with a number of different substances. I may be permitted to quote the following list from his paper, the doses in each case being 1 c.c. given twenty-four hours before infection

¹ 'Zeitschrift f. Hygiene u. Infektionskrankh.,' xvi, 1894, p. 287.

with the cholera vibrios. The animals were guinea-pigs of about 200-gramme weight.

Nature of previous treatment.	Maximal non-fatal dose.	Multiple of max. non-fatal dose for normal animal.
0. Normal	$\frac{1}{15}$ loop ¹	—
Water	$\frac{1}{3}$ loop	= 5
Urine (human)	$\frac{1}{2}$ loop	= 7.5
Bouillon (pepton)	$\frac{2}{3}$ loop	= 10
Serum (human)	$\frac{2}{3}$ loop	= 12
Nucleinic acid (2 per cent.)	1 loop	= 15
Tuberculin	1 loop	= 15
Potent cholera serum	4 loops	= 60

It will be observed how very considerable is the effect when the special or specific serum from an animal immunised against the cholera vibrio was employed. Here two factors were in evidence:—1, the increased general resistance; 2, the specific action of the cholera serum.

In the course of my experiments several different kinds of microbes have been used.

The following is an instance where typhoid bacilli were the infecting agent, and rabbits were the animals, the preliminary doses (1 c.c.) being given twenty-four hours before infection.

No.	Previous treatment.	Infected with	Result.
1	0	4 loops	Died in under 17 hours.
2	0	3 loops	Died in 9 days 22 hours.
3	1 per cent. NaCl	4 loops	Recovered after illness.
4	Typhoid serum (horse)	6 loops	Recovered; hardly ill.
5	„	9 loops	„

In other experiments guinea-pigs have been protected by sterile injections of nutrient broth against *B. coli*, *B. pyocyaneus*, and *B. prodigiosus*, as well as the above-mentioned vibrios and typhoid bacillus.

I do not propose to enter here into the anatomical details of the nature of this condition of increased resistance; let it suffice to say that the bactericidal power of the peritoneal fluid is greater than that of normal peritoneal fluid;

¹ 1 loop = about 2 mgrm.

and also that it contains a very large number of active phagocytes of two kinds,¹ which are not seen in normal peritoneal fluid.

These two facts, viz. increased bactericidal power of the fluid and increased number of phagocytes, together account for the protection which is given; supplemented by the specific substances of immunised sera when such have been administered.

In view of these facts it ought to be earnestly considered whether some similar preliminary treatment should be undertaken before operating through the peritoneal cavity upon abscesses.

In some cases contamination of the peritoneum can be avoided by operating in two stages (Sonnenburg, in appendicitis); but this is not always possible.

Two points deserve further consideration and attention. First of all, be it observed that the protection which can be afforded is *not unlimited*; it therefore follows that scrupulous care must be taken in order to make the unavoidable contamination minimal in amount,—in fact, as if no protective agency had been called into requisition.

Secondly, we have to discuss the nature of the injection which it would be profitable to employ in any given case. Here let it be understood that any suggestions on this score must be regarded as tentative, for as yet we have no actual experience in the matter in man. The point to be aimed at is TO PRODUCE AN AMPLE LEUCOCYTOSIS IN THE PERITONEAL FLUID, AND ALSO IF POSSIBLE TO GIVE A SUPERADDED SPECIFIC PROTECTION BY AN ASEPTIC INTRA-PERITONEAL INJECTION INTRODUCED ABOUT TWENTY-FOUR HOURS BEFORE PROCEEDING TO OPERATE.

If it were possible to know exactly what noxious microbes would be encountered in any given case, the obvious precaution to take would be to give a previous injection of the serum of an animal immunised against the

¹ Finely granular oxyphil or polynuclear leucocytes or microxocytes, and macrophages.—*Vide* 'Proc. Brit. Assoc.,' 1896, September 23rd; and 'Journal of Pathology,' March, 1897. (This has just come out.)

same microbe and its toxin.¹ Unfortunately we are not able to gain exact knowledge upon this point until the time of operation, and we have to rely upon more or less shrewd guesses. It becomes a matter of some importance to know *what microbes will probably be encountered*, and to guide our steps according to this probability.

To this end, I have made a number of observations upon fatal cases of peritonitis which have occurred from time to time in Guy's Hospital.

Before discussing these cases a few words may be said upon the literature of the subject.

Much evidence has been adduced to show that peritonitides and abscesses arising during the puerperium or after abortions are to be ascribed to streptococcal infection.² It would therefore be advisable, in cases of abscess having such origin, to protect the peritoneum with anti-streptococcic serum the day before proceeding to open the abdominal cavity.

Cases of cœliotomy in which a healthy peritoneum has been contaminated by the surgeon have often been shown to have been infected with staphylococci or streptococci, though in some cases other organisms have been found. However, cases of this nature are not strictly included in the class under consideration; and as far as they are concerned it can only be said that if a surgeon and his assistants, for whom he is responsible, are unable to be sufficiently cleanly, they had better desist from undertaking these as well as other operations.

In recent years great stress has been laid upon the importance of *B. coli communis* as the prime ætiological factor in cases of intestinal origin. Some observers,³ indeed, have gone so far as to use carbolised culture media (in which

¹ Anti-bacterial sera have no antitoxic action as a rule; antitoxic sera have both antitoxic and anti-bacterial action (*vide, e.g.,* Wassermann, 'Zeitschr. f. Hygiene,' 1896, vol. xxii, p. 263).

² *Vide* Hahn, &c.

³ *Vide* Malvoz; and again Laruelle, who examined two cases resulting from strangulated hernia, one of them five days after death (!); also Roswell Park.

the *B. coli* is one of the few organisms capable of growing) in order to prove their point. As a matter of fact, the difficulty is to get the other organisms and not *B. coli* to grow.

E. Fränkel (fifteen cases) and Predöhl (fourteen cases) tend to lay stress upon the presence of streptococci in these conditions.

Tavel and Lanz, who are also no enthusiastic supporters of *B. coli* as the essential factor, report twenty-eight cases with streptococci out of a total of forty-one (= 68 per cent.).

Max Oker Blom, in studying the penetration of the gut wall after experimental strangulations, remarks that various cocci were present besides *B. coli*.

Barbacci found *B. coli* in all the fourteen cases of peritonitis of intestinal origin that he examined, yet he is very careful to insist upon the fact that "although it may be the only cultivable microbe present, it cannot be regarded in the character of a truly pathogenic agent in the ætiology of perforative peritonitis."

A. Fränkel says that even with a perforated gut the peritoneum may contain pure cultures of *B. coli*; this is not in accordance with my experience, as will be seen in the record given below,—in fact, pure infection with *B. coli* appears to be a rare condition when the peritoneum is thoroughly examined, and suitable nutrient media used. I have often obtained pure gelatine plates of *B. coli* from cases in which other cultivating media yielded abundant cocci, and other forms as well.

There is much evidence that *B. coli* is pathogenic for man (abscesses, empyemata, &c.); and I am far from denying that it may have a rôle in certain cases of peritonitis, either of itself, or as a participator in mixed infections. However, in a large proportion of the cases examined, cocci (especially streptococci) were a prominent feature.

I would next divert to make a few remarks upon the method of examination. In the first place I would insist upon the importance of the examination of the *omentum*.

It has been shown¹ that substances (bacilli, Indian ink, &c.) become deposited upon the omentum after introduction into the peritoneal cavity; so much so that the peritoneal fluid may be quite sterile, microscopically and culturally, whilst upon the omentum (and other peritoneal membranes) numerous, even infinite numbers of organisms are to be found. It therefore follows that mere failure to find microbes in peritoneal fluid is not sufficient evidence to stamp a case as "chemical peritonitis" (Tavel and Lanz).² No doubt in such cases the prime cause is toxic or chemical, yet if living infective agents are still present the inference clearly is that they may have had some share in the production of the fatal dose. But a mere examination of the local condition in the peritoneal cavity is not sufficient to give conclusive evidence as to the actual pathogenic microbe which has been the cause of death.

The two places in this connection are—1. The lymph paths and glands concerned with the peritoneum. 2. The blood.

It is curious that the lymph drains of the largest lymph space in the body are not even hinted at in works on anatomy. I have pointed out elsewhere (*loc. cit.*) that the most important of the lymph channels which drain the peritoneal cavity are those which pass up along the anterior mediastinum. This is founded on the experimental evidence of the passage of bacilli and coloured materials along these tracts, and is confirmed by the dissection of a case of ruptured tubal gestation in which the lymph paths were beautifully injected with blood; as well as of observations on tuberculous and acute peritonitis, in both of which these lymphatic glands are found to be affected.

In cases of acute peritonitis the glands of the anterior mediastinum (those in the first intercostal space are the most constant and convenient to examine) are reddened,

¹ Brit. Assoc., 1896, and Gruber and Durham, 'Wiener klin. Wochenschr.,' 1896.

² The same holds good for examinations of hernial sacs and fluid, which have often been said to be sterile (*vide* Brentano).

swollen, and are found to contain microbes; sometimes they are necrotic, sometimes they are more or less hæmorrhagic. These being paths whereby microbes pass from the peritoneal cavity to the blood to cause bacteriæmia (Kocher) or general infection, it is obviously necessary to examine them.

The examination of the blood has been made by sucking some from the jugular vein with sterile pipettes. Careful antisepsis and asepsis have been employed to prevent contamination; and many control cultures have been made from non-septic cases in order to test the methods employed.

A complete examination of a case of peritonitis entails, therefore, the following investigation:—Microscopical (hanging drop and stained specimens) and cultural from peritoneal fluid, omentum, anterior mediastinal gland juice, blood, as well as examinations of the pseudo-membranous deposits and flakes ("lymph," "fibrin") which are often present, and are cellular (not fibrinous) in structure. (See Table, pp. 203, 204.)

The Cases 8, 9, 14, 17, and 19 are especially interesting in the light of A. Fränkel's investigations. This author shows that many cases which die shortly after operation, and whose deaths are ascribed to shock, are in reality cases of acute septic infection.

Observations upon animals (which may die as early as four or five hours after infection) show that the more virulent the infection the less marked are the local signs of peritonitis. In the post-mortem room, unless a quantity of pus is found in the peritoneum, the case is often put down as "no peritonitis:" observation of the omentum and the anterior mediastinal lymph tracts, combined with bacteriological examination, will set this matter right. It is only when animals die of relatively subacute peritoneal infection that pus, flakes of cells, pseudo-membranes, and the like are to be found.

[The whole question of death in comatose states, shock collapse, &c., requires further investigation. At present I have only examined one case of "uræmic coma;" in this

the blood and organs were literally swarming with *Staphylococcus aureus*. In this case the examination was made within three hours of death.]

These cases are sufficient to show that the bacteria in peritonitis are of various kinds, and that it is not possible to be certain what those kinds will be in given cases. However, it will be seen that cocci, especially streptococci, must be regarded as important infecting agents even in poly-infections of the peritoneum.

These cases, with those of the authors quoted above (Tavel and Lanz, Predöhl, &c.), and Dr. Klein's and Vincent's observations on perforation in typhoid fever (see Case 13), all point towards the advisability of the prophylactic use of anti-streptococcal serum the day before an operation is undertaken in dangerous conditions.

It will be borne in mind that the peritoneum will be strongly protected specifically against streptococcal invasion; whilst at the same time it will have an increased resisting power towards other kinds of pathogenic microbes.

It has already been shown that the varieties of *B. coli* obtained from cases of peritonitis do not all react mutually with the sera obtained by their means (Durham, loc. cit.); there is therefore no advantage in using one kind of *B. coli* serum for prophylactic injection.

Of indifferent substances nuclein or nucleic acid seems to be the most active; but as far as can be seen at present the anti-streptococcal serum promises better results.

The second point towards which I propose to call your attention is in regard to the treatment of general suppurative peritonitis. The only treatment in which the hope of saving the patient lies consists in the cleansing of the peritoneal cavity, combined with the sealing up of the source of infection if any, and possibly also the administration of a proper serum therapeutically.

It is to the matter of the technique of the flushing or washing process that I venture to direct your attention.

I have already adverted to the fact that the peritoneal

cavity rids itself of small foreign bodies (bacteria, &c.) partly by determining deposit on the omentum, &c., and partly by the intervention of the lymph flow. Also that the peritoneal fluid may contain but few microbes, or indeed be quite sterile, at a time when the omentum shows abundant hosts of them.

This was the case in the rabbit No. 2, referred to at the commencement of the paper, as well as in a number of other animals during the course of my experiments.

It appears that the peristaltic movements of the intestines are largely responsible for the deposition upon the omentum, whereby in small animals the omentum becomes rolled up. Owing to this function of the omentum being dependent upon the intestinal movements, we can readily understand the *rationale* of the otherwise empirical use of cathartics suggested by Lawson Tait; by such means the peristalsis is established, and improved circulation is determined to the mesenteric vessels, from which the chief transudation of fluids and leucocytes takes place.

In the laboratory and in the post-mortem room it is found that the majority of organisms and exudation cells are found about the omentum, the surfaces of the liver, spleen, and diaphragm,—in fact, the upper parts of the peritoneum. It seems clear, therefore, that in cleansing the abdominal cavity *especial attention should be paid to thoroughly washing and mopping these parts—the omentum, and between the liver and diaphragm*,—not that the other regions should be neglected.

In conclusion it may be said that (1) the prophylactic intra-peritoneal injection of suitable sterile material (such as anti-streptococcal serum, sterile broth, or some blend of different kinds of serum) twenty-four hours before proceeding to operations on cases where the peritoneum is in danger of being contaminated by the contents of abscesses, &c., and (2) the particular cleansing of the omentum and upper part of the peritoneal cavity, in operating upon cases of general peritonitis, both appear to be rational, and practical from being based upon experimental observations.

Finally I must express my thanks to the physicians and surgeons of Guy's Hospital for kindly allowing me to use the cases which were under their care, and express the hope that many otherwise hopeless cases may be saved by the precautions and technique which have been indicated.

The following literature may be consulted in connection with the above remarks :

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BUMM.—“ Zur Aetiologie der sept. Peritonitis,” ‘München. med. Wochenschrift,’ 1890, p. 185.

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E. FRÄNKEL.—‘München. med. Wochenschr.,’ 1890, pp. 23 and 202.

A. FRÄNKEL.—“ Ueber peritoneal Infection,” ‘Wiener klin. Wochenschr.,’ 1891.

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M. HAHN.—“ Ueber die Steigerung der natürlichen Widerstandsfähigkeit durch Erzeugung von Hyperleucocytose,” ‘Berlin. klin. Wochenschr.,’ 1896, p. 864.

M. HAHN.—“ Ueber die Beziehungen der Leucocyten zu baktericiden Wirkung des Bluts,” ‘Arch. für Hygiene,’ xxv, 1895, p. 105.

KLECKI.—“ Recherches sur la Péritonite d'Origine intestinale,” ‘Annales Inst. Past.,’ ix, 1895, p. 710.

LARUELLE.—“ Étude bactériologique sur la Péritonite par perforation,” ‘La Cellule,’ v, 1889, p. 61.

LOISON.—“ De l'appendicite ulcéro-perforante,” ‘Rev. de Chirurgie,’ xv, 1895, p. 1.

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TAVEL AND LANZ.—“Ueber die Aetiologie der Peritonitis,” ‘Mittheil aus Kliniken u. med. Inst. der Schweiz,’ 1893.

TREVES.—“Lettsomian Lectures on Peritonitis,” ‘Brit. Med. Journ.,’ 1894.

VINCENT.—“Étude sur les Résultats de l’Association du Streptocoque et du Bacille Typhique,” ‘Ann. Inst. Pasteur,’ vii, 1893, p. 141.

WURTZ AND HERMANN.—“De la Présence fréquente du *B. coli* dans les Cadavres,” ‘Arch. Méd. Exp.,’ 1891, p. 734.

Postscript.—Dr. Muscatello, of Turin, has sent me a copy of his paper on “Absorption from the Peritoneal Cavity” (‘Virchow’s Archiv,’ cxlii, 1895). In this he calls attention to the importance of the lymphatic tracts of the anterior mediastinum; and I must offer an apology for having overlooked his valuable contribution.—*April*, 1897.

(For report of the discussion on this paper, see ‘Proceedings of the Royal Medical and Chirurgical Society,’ Third Series, vol. ix, p. 91.)

No.	Sex.	Age.	Diagnosis, &c.	Since Death.	Bacteriological Examination, &c.
1	F.	13½	Double suppurative salpingitis; suppurative peritonitis; caeliotomy; lavage; drainage. Death after 9 days	14 hours	Bacillus coli; streptococci; blood sterile to broth culture.
2	F.	9	Perityphlitic abscess; operation. Death 4th day; suppurative peritonitis	19 hours	Bacillus coli; streptococci.
3	M.	15	Perityphlitic; perforated appendix; general suppurative peritonitis; operation not undertaken	3 hours	Streptococci very abundant; a few large non-liquefying bacilli; only streptococci from anterior mediastinal gland.
4	M.	7	Perforated appendix; suppurative peritonitis; no operation	3½ hours	Abundant small bacillus unidentified; few B. coli; few cocci.
5	M.	42	Recurrent attacks; ulcerative colitis; suppurative peritonitis; no operation	19 hours	Poly-infection; streptococci very abundant; bacillus growing in long threads, abundant; some B. coli.
6	F.	64	Strangulated femoral hernia; bowel gangrenous; primary resection; Murphy's button. Death 4th day; suppurative peritonitis	47 hours	Poly-infection locally; several kinds of bacilli, also streptococci; ant. med. gland pure culture streptococci; blood sterile to culture.
7	F.	42	Strangulated umbilical hernia; resection, Murphy's button. Death 10 hours after operation = 33 hours after strangulation	24 hours	All organs crammed with large, anaërobic, non-motile bacillus, also small bacillus which did not grow; ant. med. gland very red, swollen, and soft.
8	F.	41	Femoral strangulated hernia; perforation; resection, Murphy's button; acute peritonitis. Death within 24 hours	4 hours	Peritoneal fluid sterile; omentum and anterior med. glands abundant Staphylococcus aureus; blood sterile.
9	M.	10	Intussusception; caeliotomy; "collapse;" death. Several operations, death 15 hours after last; acute peritonitis	9 hours	Abundant B. coli and staphylococci.
10	M.	2½	Intussusception; caeliotomy; Murphy's button. Death	24 hours	B. coli and streptococci; droplet of juice of ant. med. gland remained sterile.

No.	Sex.	Age.	Diagnosis, &c.	Since Death.	Bacteriological Examination, &c.
11	M.	64	Epithelioma of cæcum; obstruction; peritonitis; no operation. Death	25 hours	<i>B. fluorescens</i> non-liquefaciens (much like <i>B. coli</i> for 4 or 5 days) and staphylococci.
12	M.	56	Epithelioma recti; inguinal colotomy; suppurative peritonitis. Death	17 hours	Locally abundant streptococci and small bacillus; anterior med. gland only cocci.
13	M.	24	Enterica; perforation. Death.	8½ hours	Locally poly-infection; especially abundant streptococci; also <i>B. coli</i> and other bacilli.
14	F.	58	Epithelioma pharyngis; gastrostomy; "exhaustion." Death 40 hours after operation	15 hours	Very abundant streptococci; also <i>B. coli</i> .
15	F.	23	Gonorrhœal pyosalpinx; celiotomy; suppurative peritonitis	31 hours	Cocci and bacillus resembling <i>B. coli</i> , but which slowly liquefied gelatine; ant. med. glands only cocci, which did not grow.
16	F.	63	Twisted ovarian tumour; celiotomy; "diabetic coma." Death 4th day; limited examination	12 hours	Microscopically cocci; only gelatine cultures made, which did not grow.
17	F.	41	Fibroids; celiotomy; 4th day intestinal obstruction due to kinking; operation. Death after 3 hours	11½ hours	Locally ant. med. gland and blood yielded pure growth of <i>Staphylococcus aureus</i> ; also abundant microscopically.
18	F.	22	Abscess around pyosalpinx; rupture; suppurative peritonitis	15 hours	Locally poly-infection; <i>B. coli</i> and cocci; blood and ant. med. gland pure <i>Staphylococcus aureus</i> .
19	F.	28	Suppurating ovarian cyst; celiotomy; escape of pus into peritoneum. Death 30 hours post operationem	12 hours	Locally, and ant. med. gland <i>Staphylococcus albus</i> .
20	F.	48	Sloughing fibroids; pelvic abscess; celiotomy. Death 3rd day; acute peritonitis	3 hours	Locally streptococci and staphylococci; blood pure <i>Staphylococcus citreus</i> .