Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Peritoneal Immunization

Volume XII | Friday, March 14, 1941 | Number 20

STAFF MEETING BULLETIN
HOSPITALS OF THE . . .
UNIVERSITY OF MINNESOTA

Volume XII | Friday, March 14, 1941 | Number 20

INDEX

Published for the General Staff Meeting each week during the school year, October to May, inclusive.

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William A. O'Brien, M.D.

I. LAST WEEK

Date: March 7, 1941

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:00 P.M.

Program: Movie: "Mickey's Trailer"

Biliary Stricture
John R. Paine

Discussion
Clarence Dennis
C. J. Watson
Charles E. Rea

Present: 141

Gertrude Gunn
Record Librarian

- - -

II. MOVIE

Title: "Modern Nursing Technique"

Released by: Eastman Company

- - -

III. ANNOUNCEMENTS

1. No meeting next week, Friday, March 21, 1941 because of Spring vacation. There will be a meeting two weeks from today on Friday, March 28.

2. MOVIE today is concerned with aseptic nursery technique as used at The Cradle in Evanston. It tells the story of the efforts made by this institution to prevent hand- and air-borne cross infections. In 1927 an epidemic of enteritis broke out at The Cradle. 80 infants contracted the disease, 27 of whom died.

Thereupon, a scrupulous technique for the control of hand-borne cross infections was developed by Dr. Gladys Dick. The following figures show the results: among the 2669 infants admitted to The Cradle from 1929 to 1939, there were 42 with diarrhea, 48 with impetigo and 8 with gonorrheal vaginitis. No instance of cross infection was observed. The ten-year period proved that this individual aseptic nursery technique had solved the problem of hand-borne infections at The Cradle.

Basic principle for the prevention of cross infection include control of the following:

1. Skin infections, such as impetigo.
2. Gastrointestinal infections, such as dysentery.
3. Venereal infections, such as gonorrhea and syphilis.
4. Contagious diseases, such as chicken-pox and whooping cough.
5. Respiratory infections, such as colds, bronchitis, and bronchopneumonia.

The modes of transmission of the above diseases are:

1. By contact:
   a. Direct - from infant to infant
      from infant to nurse
      from nurse to infant
      from nurse to nurse
   b. Indirect - by contaminated objects such as gowns, nipples, food, bath tub, thermometer, etc.
2. By air currents.

In order to prevent the spread of these infections The Cradle has developed Units completely separated from each other with individual nursing staffs and individual cubicles for each infant in the unit. Special features to prevent air-borne infection are the use of air condition, germicidal light, and mechanical barriers. The mechanical barrier units were designed by James A. Reyniers of the University of Notre Dame. In the technique program the following procedures are observed: scrubbing and disinfecting hands and forearms, care of infected nurses and other attendants, and special procedures for the prevention of gastrointestinal infection (feeding nurses feed the infants while diaper nurses weigh and bathe the infants, and change all diapers.....

IV. PERITONEAL IMMUNIZATION AND THE TREATMENT OF PERITONITIS

Charles E. Rea

Peritonitis is the chief complication that surgeons dread in abdominal surgery. Much experimental work has been done on the production and prevention of peritonitis in animals, with attempts to correlate these findings with the prevention of peritonitis in human beings. The purpose of this report is to compare the relative efficacy of certain substances in preventing peritonitis in rabbits.

In general, peritoneal protection may be produced by five methods:

1. Intraperitoneal use of certain drugs and antiseptics.
2. Introduction of a vaccine into the peritoneal cavity, producing a general immunity in which the peritoneum shares (true immune process).
3. Anti-bacterial sera (passive immunity).
4. Local protection of the peritoneum attributable to a local hyperleucocytosis and afforded by the intraperitoneal introduction of any number of vaccines and other substances.
5. Use of agents as deep X-ray therapy.

Intraperitoneal use of certain drugs and antiseptics.

While certain chemicals may kill organisms in vitro, when introduced into the peritoneal cavity, they often cause more irritation than good. Recently the use of sulfanilamide has enjoyed some popularity. Garlock and Seley believe the incidence of peritonitis following operations on the colon is decreased if sulfanilamide is given for three days preceding operation and for several days thereafter. Ladd, Botsford and Curnen state that the high mortality rate in primary peritonitis in infants and children can be markedly reduced by early operation and drainage followed by adequate treatment with sulfanilamide in the streptococcal group and type-specific serum in the pneumococcal group. Ravdin and his co-workers found that the mortality in appendicitis with peritonitis was lowered from 1.4 to 0.4% following the use of this drug. Corry, Brewer and Nicol report similar results in the treatment of peritonitis of appendical origin with sulfanilamide. However, it is unfortunate that peritonitis secondary to appendicitis was used as the test case, as in our experience even in cases of generalized peritonitis of appendical origin, 60% of the cases recover with conservative therapy (Sperling and Myrick).

Our interest in the possible use of sulfanilamide intraperitoneally dates back to 1938, when Jensen and his co-workers found that the incidence of infection in compound fractures was less when sulfanilamide was placed in the debrided wound.

At the University of Minnesota Hospitals, sulfanilamide in divided doses of four to six grams a day is given subcutaneously in most cases of peritonitis irrespective of its origin. On three occasions ten grams of sulfanilamide were poured into the peritoneal cavity at laparotomy when peritonitis was present. While all the patients were critically ill at the time of operation, the fact that two of the patients died made us cautious as to the further use of sulfanilamide intraperitoneally in such doses when peritonitis was already present. At present sulfanilamide in doses of 3 to 4 grams is placed in the peritoneal cavity of selected patients where there has been actual or suspected contamination at operation. The powdered sulfanilamide is dusted around the anastomotic sites (3 to 4 grams) and an additional two grams are sprinkled also in between the different layers in closing the abdomen. Varco, in this experimental laboratory, has shown a distinctly lowered mortality rate in dogs following complicated gastro-intestinal anastomosis when sulfanilamide was used intraperitoneally (unpublished data). Experimental work will be presented in this paper

which shows that the "pre-peritonitis" use of sulfanilamide is of some value.

The use of intraperitoneal vaccination and substances to produce an intraperitoneal hyperleucocytosis.

In 1894 Issaef introduced the idea of vaccination to prevent postoperative peritonitis. Pierralini in 1897 found that a leucocytic exudate could be produced by the intraperitoneal injection of saline solution and other inert substances. Garnier demonstrated that bacteria were rapidly destroyed in the presence of a leucocytic exudate in the peritoneal cavity; his studies showed the importance of phagocytosis in protecting the patient from peritonitis. In 1902, Solieri produced a peritoneal leucocytic exudate in animals and found that animals with such an inflammatory reaction of the peritoneum survived a colon bacillus peritonitis.

In 1922, Johnson first used amniotic fluid to prevent postoperative adhesions and later to protect against peritonitis. He explains the action of amniotic fluid on the peritoneum as one that produces a protective layer of fibrin on the serous surfaces and a moderate local leucocytosis which is followed later by a complete resolution of the fibrinous deposit. He describes the peritoneal reaction as a defense response characterized by hyperemia, marked subserous edema, increase in the peritoneal fluid and the formation of a pink-tinged fibrinous exudate. There is an increased white cell count that rises rapidly for about 12 hours, at which time the differential count shows a marked preponderance of polymorphonuclear leucocytes. Following this peak, the neutrophils are replaced by histiocytes until the cell count becomes predominately histiocytic. If the exudate is removed from the peritoneal cavity it forms a fibrinous clot. The peritoneal exudate following intraperitoneal injection of vaccines is profuse and hemorrhagic and does not clot when exposed to air.

Steinberg and Goldblatt began their extensive work on peritonitis in 1926. They showed that intraperitoneal immunization by living and heat-killed colon bacilli produced an immunity in animals to subsequent colon bacillus and fecal peritonitis. They presented convincing evidence that when colon bacilli in saline suspension were injected intraperitoneally they were rapidly absorbed into the blood and lymph but such animals practically always survived. However, when equal doses of colon bacillus were suspended in 1% gum tragacanth, the animals did not get a bacteremia but invariably died. One explanation of this was that toxic products of the bacteria were formed in quantity only when they were retained within the peritoneal cavity and that these toxic products caused the death of the animal.

David and Sparks in 1927 showed that when colon bacilli were injected intraperitoneally they passed readily into the blood and lymph. However, when a plastic peritonitis was first produced by injection of a turpentine emulsion, organisms subsequently injected intraperitoneally could not be recovered from the blood or thoracic lymph.

Herrman in 1927 showed that in order to produce a peritoneal exudate in rabbits it was necessary to first build up an immunity before injecting the infecting material. This was successfully carried out by using repeated small intraperitoneal doses of a vaccine prepared from the colon bacillus and streptococcus viridans. At autopsy the animals showed a true fibrinopurulent peritonitis, but control animals receiving no such immunizing vaccine died with no signs of peritonitis.

In 1931, Morton injected various substances into the peritoneum, such as dextrose broth, heated streptococcic filtrate, various solutions of glucose and saline. Using rabbits he found that he was able to establish a certain degree of protection in most of the animals.

Rice, in 1933, attempted to immunize the peritoneum of dogs by injecting intraperitoneally a mixture of staphylococcus, streptococcus and B. coli bacteriophage filtrates. The animals were given the bacteriophage before or

at the time of operation which consisted of tying off the cecum in order to produce peritonitis. Bacteriophage failed to immunize the peritoneum in his experiments; moreover the formation of plastic exudate seemed to be inhibited. Jern, Harvey and Meleney, working with mice, reported the effect of bacteriophage on peritonitis due to B. coli. They were able to protect the animals against such an infection even when they used doses twenty-five times the size of the lethal doses for controls. The phage was effective when used intraperitoneally before, during or even several hours after the injection of colon bacilli.

Bacteriology of peritonitis.

Roberts, Johnson and Bruckner maintain that in the vast majority of human cases the peritoneal cavity is not sterile. They obtained positive cultures in 76% of their cases in which the peritoneum was opened in clean operation. However, these organisms were practically the same as those which they obtained from the deep layers of the skin before the peritoneal cavity was opened, which would seem to indicate their source. The organisms were chiefly diphtheroids or staphylococci which were also found in the laboratory air. Rather surprising was their finding that cultures from frank infections of the peritoneal cavity did not yield a much higher per cent of positive cultures than cultures from the non-inflamed cavity.

The colon bacillus seems to be the commonest organism encountered in peritonitis of intestinal origin. In 1891, Malvoz stated that peritonitis of intestinal origin should not be attributed to any bacteria other than B. coli. In 1938 Altemeier reviewed the literature of the bacteriology in perforated appendicitis. Most of the authors quoted by Altemeier believed B. coli to be the commonest organism encountered, although he found the bacterial flora in some cases to be very complicated and bizarre. Owen studied cultures or peritoneal fluids of animals injected intraperitoneally with suspensions of total cecal contents of normal animals, usually the guinea pig. Such cultures revealed members of the coliform group of bacteria in 51% of the cases. Cultures from animals dying of the infection showed the organisms in 84% of the cases while in animals that survived 16% of the cases showed these organisms. Streptococci were seldom found and pathogenicity tests gave comparatively low death rates. Mixed cultures of streptococci and coliform organisms killed some animals but the streptococci could seldom be found in the peritoneal fluids of animals dead of these injections.

Cellular Exudate in Peritonitis

It has been established from animal experiments and clinically in patients that the introduction of foreign substances into the peritoneal cavity will excite the production of a defensive cellular exudate. The contents and volume of this exudate will be determined to a large extent by the character and amount of the substances involved. This reaction is characterized locally by hyperemia, increase in the peritoneal fluid, increase in the histiocytic and leucocytic counts and phagocytosis.

There is no uniformity of opinion as to the relative protective functions of the polymorphonuclear leucocytes and the histiocytes. Steinberg regards the polymorphonuclear as the important phagocytic cell and feels that the histiocyte is a scavenger cell which appears late in peritonitis when it engulfs the degenerated polymorphonuclear leucocytes. Coller and Brinkman also believe that the polymorphonuclear leucocyte is the important cell in phagocytosis. Johnson, et al, believe that the histiocyte is a superphagocyte and comes into the picture late in response to dead tissue. However, Herrman expressed his belief that the histiocyte is probably the most important cell concerned with phagocytosis.

Garnier, Wilkie, Coller and Brinkman found examination of the peritoneal exudate to be of value in determining the progress of acute peritonitis. It should be emphasized, however, that local immunity cannot be measured in terms of one total or differential leucocytic count

alone. Other factors, chiefly humoral, play an important part (Johnson, McCollum).

In 1938, Rixford studied the peritoneal fluid of patients at operation who had previously received intraperitoneal vaccine and compared these findings with a control group of patients who had received no vaccine. Specimens were taken with a glass pipette just after the peritoneal cavity was opened. In unvaccinated cases, the total white cell count averaged from 1900 to 2600 per cu. mm. of fluid. There were practically no neutrophils, very few eosinophils and basophils, but many lymphocytes and histiocytes (45%). In patients who had been vaccinated 24 to 144 hours prior to operation, specimens of peritoneal fluids were also examined. There was considerable variation in the findings but it was apparent that there was an early increase in polymorphonuclear cells and a delayed but marked increase in histiocytes.

Seeley, Higgins and Mann observed the cytologic response of the peritoneal fluid of rats to injections of amniotic fluid concentrate, Bargen's vaccine (prepared from colon bacilli and non-hemolytic streptococci) and sodium ricinoleate. They found that with all materials there was an early and rapid rise of polymorphonuclear leucocytes, reaching a maximum in three to six hours. Histiocytes appeared much later, but were the preponderant cells after six or seven days. The response of both cells was greater in those animals receiving sodium ricinoleate.

In 1937, Corwin reported that in the rabbit, the cellular responses to Bargen's vaccine and sodium ricinoleate were nearly identical qualitatively. However, with Bargen's vaccine the cell count of the peritoneal fluid was greatest at 12 hours, with 1% sodium ricinoleate at 24 hours and with 2% sodium ricinoleate at 48 hours. The differential count showed the polymorphonuclear to appear early, being in greatest abundance in six to twelve hours, while the histiocytes were maximal in 1 to 3 days. Whereas the cell count per cubic millimeter after injection of sodium ricinoleate was only 40,000, the total amount of fluid was so much greater that a greater total number of cells was evoked by the ricinoleate than by Bargen's vaccine.

Coller and Rife in their review of the cellular aspect of immunization believe that the variation in opinion regarding the relative phagocytic properties of the neutrophil and histiocyte is due in part to the use of different species of animals by different workers. Also the type of material used, the dosage employed, the time intervals for examination of the fluids are not constant in the different studies.

Clinical results following the use of intraperitoneal vaccines and other substances.

Steinberg and Goldblatt developed a protective emulsion consisting of Escherichia Coli in tragacanth, which they call coli-bactragen.* This substance will protect the experimental animal from certain types of subsequently-induced peritonitis. Steinberg has demonstrated protection against living colon bacilli, streptococcus fecalis, B. pyocaneus, and Cl. Welchii, in both pure and mixed cultures.

In 1934 Goldblatt reported a collected series of 400 patients receiving coli-bactragen. Eight postoperative deaths were recorded but only three of these could be attributed to peritonitis. The operations were performed by various surgeons and consisted chiefly of resections of the large bowel. The first preparation of coli bactragen was injected intraperitoneally about 24 hours before operation and was frequently accompanied by a rather severe general reaction. The more recent preparations of coli bactragen produce a less severe general reaction and achieve its maximum protection within a few hours.

In 1934, Potter and Coller reported a series of 79 patients, most of whom had major operations performed upon the colon, who were given coli bactragen before

*Coli-Bactragen (Steinberg) consists of 50 million bacteria per 30 cc. with 1% of 1:10,000 merthiolate suspended in 1.5% gum tragacanth.

operation. There were 11 deaths, in only one of which was the lethal outcome attributed to peritonitis. Although the series was small and not controlled, they were of the opinion that vaccine was probably not indicated except in cases of gross fecal contamination. In 1936, Coller and Ransom reported the use of coli bactragen in 79 cases which had a combined abdomino-peritoneal resection for carcinoma of the rectum and rectosigmoid. There were 12 deaths, but in none was death believed to be due to peritonitis. In the same year Steinberg reported 391 cases in which coli bactrogen was used preoperatively or at the time of operation with none developing postoperative peritonitis.

In 1928, Bargen developed his vaccine prepared from streptococci and colon bacilli. It was given intraperitoneally three days before intestinal operations. In 1935 Dixon and Bargen reported 1500 cases in which the vaccine had been used with a reduction of 66% in the mortality rate from postoperative peritonitis. The vaccine was attended with degrees of general systemic reaction. In 1930 Rankin in a review of 527 surgical lesions of the large intestine and rectum in which peritoneal vaccination was used preoperatively reported a mortality rate of 12.3% by patient and 8.6% by operation. In 1933, he reported a new series in which the vaccine was not used. In 200 consecutive operations upon the colon and rectum, he reported a mortality of 5.5% by operation and 8.4% by patient. He attributed the decline in mortality to better preoperative preparation rather than to vaccination.

Johnson, Warren, Trusler, Young and Marks, Klimpton and others have reported their results using amniotic fluid concentrates. Young and Mark reported upon the use of amniotic fluid concentrates in 49 cases which involved chiefly operations on the colon. There were three deaths, but in only one instance could death be attributed to postoperative peritonitis. In a series of 46 similar cases in which amniotic fluid was not used preoperatively there were 8 deaths (17.3%). In the cases of colonic reaction the mortality was 38% in the control series. Gepfert believes the postoperative convalescence is smoother in patients receiving amniotic fluid.

Serum

Many clinical studies have appeared in the literature concerning the treatment of peritonitis with various sera. Very little experimental work has been done, however. It is impossible to tabulate or evaluate different series as the type of serum and method of administration vary widely.

The following antigens have been employed: (1) bacillus-coli filtrate, (2) toxins of Cl. Welchii or of combined anaerobes, (3) a combination of colon and gas bacillus, (4) enterococci, usually added to colon bacili and anaerobes, (5) bacterial bodies as well as colon and gas bacilli, (6) a number of other organisms such as the bacillus fusiformus, bacillus fundiliformus, staphylococcus, and intestinal streptococci which have produced a serum to which is added polyvalent antigas-gangrene serum and anti-coli serum (Harvey and Meleney).

It should be mentioned that not all the anaerobes found in the exudate in peritonitis are virulent. Also, it is not known that a serum produced against one strain of bacillus coli will be effective against other strains of the same organism. For these reasons, it is doubtful that potent sera can be produced commercially according to our present knowledge.

The first use of bacillus-coli serum has been attributed to Guthrie (1915); he used serum together with coli vaccine only in cases which underwent operation and in which the diagnosis was doubtful. Most of the reports of the clinical use of serum have been in the foreign literature (Vincent, Weinberg, Riemann, Kunz, Pellegierri). In this country Priestley and MacCormack reported favorable results in a small group of cases.

One of the best reports is that of Riemann. He reported 368 cases of peritonitis in which either coli serum or a combined "peritonitis serum" was used during the period from 1931 to 1933. He

saw no difference in results from the two types of sera. Of 368 cases of peritonitis, 244 followed appendicitis with a 4.5% mortality and 124 followed other lesions with a 20.9% mortality. In previous three year periods without the use of serum the mortality has been from 21.7% to 22.5% for peritonitis following appendicitis and from 37.7% to 38.4% for peritonitis following other causes. Riemann never used over 100 cc. of serum in treating a case. On the other hand, Kapel of Copenhagen and Urech of Switzerland, after a fairly extensive clinical trial, found no benefit from serum in cases of peritonitis. Santi had the opportunity to try serum in 14 cases in which for one reason or another an operation was not attempted. Nine of 14 patients died.

Perrando and Chiari and Kunz, Trusler and Moss have reported experimental evidence showing that antiserum gives some protection against peritonitis. However, the series of animals was small and the specificity of the antisera not proved.

Deep X-ray therapy in the treatment of peritonitis.

For many years, deep X-ray therapy has been used in the treatment of acute and chronic infections. The use of deep X-ray irradiation in the treatment of gas bacillus infections has quite a vogue at the present time. There are occasional case reports concerning the treatment of pneumonia, peritonitis, cellulitis, etc., by irradiation, but most of these are poorly controlled and irradiation was not the only form of therapy used in many instances.

Pratt reported that the preoperative irradiation of the abdomen and pelvis of patients with carcinoma of the colon reduces the incidence of peritonitis. Kelly and Dowell advise irradiation of the abdomen in some patients with peritonitis due to rupture of the appendix. Altemeier and Jones believe roentgen therapy to be of value in immunizing animals against peritonitis. The maximum degree of immunity in animals occurred from 4 to 6 weeks after irradiation. As Blalock remarks, it is too early to appraise the value of this type of therapy at the present time.

Desjardins, from clinical observations and an extensive review of the experimental and clinical reports on the treatment of inflammations with X-rays suggests that the leucocytes undergo lysis when irradiated and in this lytic process antibodies are freed in the infected area. Kelly agrees with this idea. Experiments concerning the use of deep X-ray therapy in the treatment of peritonitis in rabbits will be discussed later.

It is difficult to evaluate the efficacy of these various agents in preventing peritonitis in clinical cases because factors such as the type of case, the drug and dosages used, time interval, etc., vary so widely. Moreover, it is not justifiable to use critically sick people as controls.

Results of certain operative procedures at the University of Minnesota Hospitals.

To evaluate clinically any substance to prevent peritonitis, one is guided chiefly by the mortality rate with and without the substance. The mortality rates for certain operative procedures at the University of Minnesota are accordingly reviewed.

1. Gall bladder disease.

From 1937 to 1940 inclusive, there has been no death in 91 consecutive cholecystectomies for uncomplicated chronic cholecystitis and cholethiasis. During the same period, however, for operations for common duct stone, there have been 4 deaths in 43 cases. These deaths were due respectively to hemoperitonemia sepsis from liver abscess, gas bacillus infection, and hepatic insufficiency with bronchopneumonia. The use of any preventative against peritonitis would have very limited indication in these cases.

2. Perforated peptic ulcer.

There were 31 patients with gastric or duodenal ulcer perforated into the free peritoneal space. There

were seven deaths. Routinely sulfanilamide or sodium ricinoleate is placed in the peritoneal cavity of such patients after closing the perforation.

3. Carcinoma of the rectum.

From 1937 to 1940 inclusive there have been 40 operable cases of carcinoma of the rectum which have been treated by colostomy and posterior excision of the rectum without a death. The other operative procedures have been listed below.

Procedure	No. of Cases	No. of Deaths
Colostomy and post excision (operable)	40	0
Colostomy and post excision (inoperable)	1	1
Abdominal perineal	1	1
No treatment	6	2
Colostomy (inoperable)	27	2
Irradiation	7	0
Fulguration only	6	0
Colostomy ± fulguration ± irradiation	13	0

Most of the operators at these hospitals sprinkle 4 to 6 grams of sulfanilamide in the post excision wound at the end of the operation, but the incidence of primary healing does not appear to be increased. Nearly all of these wounds show some signs of infection and heal by secondary intention.

1. Appendicitis.

At the previous hospital report, the results of treatment of appendicitis were reported (Dennis and Mears). From 1935-1939 there were 68 cases of perforated appendicitis with generalized peritonitis with 13 deaths (19.1%). In the same interval there were 139 instances of perforated appendicitis with localized peritonitis with 4 deaths (2.9%). In the past 2 - 3 years, oral and para oral sulfanilamide has been used in these cases.

From 1932 - 1935 there were 107 instances of perforated appendicitis with localized peritonitis with a mortality of 3.7% and 68 cases of ruptured appendicitis with generalized peritonitis with a mortality of 33.8%. The lowering of the mortality in this last group by one-third is not due solely to the use of chemotherapy but also to better selection of cases and appreciation of the indications and limitations of conservative therapy. The last 25 cases of perforated appendicitis with localized or spreading peritonitis treated conservatively and with sulfonamides at this hospital have been reviewed. One is not impressed that the temperature, pulse, leucocytic count, general condition of the patient were much different in these cases than in a similar series treated in 1935-37 not receiving sulfonamides.

Experimental data.

It is difficult to evaluate the efficacy of various agents in preventing peritonitis in clinical cases because factors such as the type of case, the drug and dosage used, time interval, experience of the surgeon, type of procedure, etc. vary so widely. Moreover, it is not justifiable to use critically sick people as controls.

In all immunologic studies it is important to realize that all immunity is relative in both a qualitative and quantitative sense; that is, if the dose or virulence of the organism is greater than the protective titre of the substance to be tested, the animal will die. Therefore, experimentally, unless quantitative as well as qualitative factors are controlled, the results are relatively meaningless.

Method

The peritoneal exudate from patients dying of peritonitis was chiefly used. This material was collected and the organisms examined as to number and identity. Several loopfuls of the material were inoculated into liver peptone broth. After 24 hours of incubation, a smear was made and stained by Gram's method. A loopful of the liver peptone culture was streaked upon blood agar and eosin-methylene blue plates for identification of organisms. Another loopful was inoculated into a tube of sterile milk and incubated at 37 degrees C. for six to twenty-four hours for determination of anaerobes.

To count the number of bacteria, the culture was drawn up to a mark on a capillary pipette; blood was drawn up to the same mark and the contents of the pipette blown out on a slide and mixed. A smear was made and stained by Wright's method. The number of bacteria and red cells in 100 fields were counted and averaged. The number of bacteria were calculated by proportion.

$$\frac{\text{Average number of bacteria per field} \times \text{erythrocyte count per cu. cm.}}{\text{Average number of rbc per field}} = \text{No. of Bacteria per cc.}$$

Full grown, stock rabbits were used as the experimental animal. In each case the culture used was 24 hours old. In a few experiments the rabbit was anesthetized with drop ether, the abdomen opened under sterile precautions and the culture was placed in the peritoneal cavity followed by the drug to be tested. In most of the experiments, however, the culture was injected into the peritoneal cavity of unanesthetized rabbits followed after a few minutes' interval by an injection of the drug through the same needle. Control experiments were carried out. The animals were observed up to a period of two weeks following injection.

The survival rate was studied as well as the incidence of peritonitis, as the animals that survived the two-week period were not sacrificed to see if they had peritonitis. Animals that died within 24 hours after injection of the culture showed little evidence of peritonitis and probably died of a bacteremia.

The following substances were tested: Sodium ricinoleate 1% as prepared by Prof. W. P. Larson, Department of Bacteriology, University of Minnesota Medical School, ether U.S.P., Tr. merthiolate, mercurochrome 2% (aq), S. T. 37, Hcl 0.5%, Hcl 1%, cow serum, coli-bactragen (Steinberg), immune rabbit serum from two sources, amniotic fluid conc (Eli Lilly), sulfanilamide. Bovine serum was tried because of the well known resistance of the animal to peritonitis. Immune rabbit serum was obtained as follows: A cardiac puncture was performed on rabbits that survived 10-14 days following the injection of a peritoneal exudate. After centrifuging the clotted blood, agglutination titre of the pooled serum against E. Coli was determined. This serum was injected intravenously into other rabbits to note its protective power against peritonitis. This is, in essence, an immuno-transfusion. "Hyperimmune" serum was made from blood of rabbits that survived five injections (2.5 cc. each) of a purulent peritoneal exudate given over a period of two weeks. This exudate contained E. Coli and streptococcus viridans, 250,000,000 organisms per cc.

Results of Experiments

Regardless of the organism used, it was impossible to protect over one-half of the animals against peritonitis. Sodium ricinoleate 1%, colibacterogen and amniotin were about equally effective. About 80% of the animals could be protected against peritonitis by the intravenous injection of hyperimmune serum. A feasible method of obtaining hyperimmune serum against peritonitis in man has not been worked out. The results obtained with sulfonamides were impressive but it may be questioned if the results obtained were significantly better than those obtained with sodium ricinoleate, colibacterogen, etc.

Sulfanilamide would seem to be most effective in the preperitonitis stage. Once peritonitis has developed, its efficacy is much reduced. Moreover, the direct application of sulfanilamide would seem to be more effective than the subcutaneous administration of the drug or placing an equivalent amount of the powder under the skin.

Present Practice at the University of Minnesota Hospitals in Cases of Peritonitis.

At this clinic sulfanilamide in doses of 3 grams has been placed in the peri-

toneal cavity at operation where there was suspected or actual contamination. If frank purulent peritonitis is present, sulfanilamide is not only of little value because it will be inactivated by the protein of the exudate, but it is contraindicated as it may aggravate a hepatitis already caused by the peritoneal infection. Clinically sulfathiazole may prove to be more effective than sulfanilamide in the treatment of peritonitis, as the former is less toxic to the liver.

In "clean" cases, there is no indication for the use of any of these agents. In clean incisions of the skin in dogs, sulfanilamide affords no higher incidence of healing by primary intention (Jensen and Rea, unpublished data).

In "dirty" or grossly infected wounds, sulfanilamide is valueless, unless a thorough debridement or cleaning of the wound is performed first. Jense, Nelson and Johnsrud found that sulfanilamide was most effective in compound fractures before there was any sign of gross infection. Moreover, in infected compound fractures, if sulfanilamide were placed in the wound before debridement or a thorough cleansing, no benefit was obtained. Similarly, in peritonitis, sulfanilamide is most effective in the pre-peritonitis stage. When peritonitis is present, its value is questionable.

Conclusions

1. In reviewing the literature, many agents have been used in treating peritonitis.

2. Clinically it is difficult to judge the value of certain substances in preventing peritonitis, as factors such as the amount and type of contamination at operation, organisms present, type of operative procedure performed, the experience of the surgeon, the condition of the patient, etc., have to be considered.

3. In experimental peritonitis, unless qualitative and quantitative factors, such as the number and type of organisms present, are controlled, the results are meaningless.

4. In these experiments, the effect of certain substances in preventing peritonitis in rabbits was studied, controlling the number and type of organisms injected to cause the peritonitis. Unfortunately the same culture could not be used in all the experiments. Of the substances tested, however, none was effective in more than fifty per cent of cases. Sodium ricinoleate, coli-bactragen and the sulfonamides were the most effective of the substances tested. It may be questioned if sulfanilamide is superior to the other substances tested in preventing peritonitis.

5. Regarding the use of sulfanilamide in the peritoneal cavity:

   a. It is not indicated in clean cases.

   b. It is most effective in the pre-peritonitis stage.

   c. It is more effective if placed in the peritoneal cavity than if placed under the skin.

   d. It is of relatively little value in cases of frank purulent peritonitis.

References

1. Garlock, J. H. and Seley, G. P. Surgery, 1939, 5:787.

2. Ladd, W. E., Botsford, T. W., and Curnen, E. C. J.A.M.A., 1939, 113:1455.

3. Ravdin, I. S., Rhoads, J. E., and Lockwood, J. S. Ann. Surg., 1940, 111:53.

4. Sperling, L. and Myrick, J. C. Surgery, 1937, 1:255.

5. Harvey, H. D. and Meleney, F. L. Surg., Gynec. & Obst., 1938, 67:339.

6. Coller, F. A., and Rife, C.
Am. J. Surg., 1939, 46:61.

7. Issaef quoted by Coller and Rife.

8. Pierrelini, G.
Ann. Inst. Pasteur, 1897, 11:308.

9. Garnier, M.
Ann. Inst. Pasteur, 1897, 11:767.

10. Soleri, S.
Beitv. z. Path. Anat. u. z. Allg. Path., 1902, 31:536.

11. Johnson, H. L.
Am. J. Surg., 1936, 34:266.

12. Johnson, H. L.
Surg., Gynec. & Obst., 1936, 62:171.

13. Steinberg, B. and Goldblatt, H.
Arch. Int. Med., 1927, 39:449.

14. David, V. C. and Sparks, J. L.
Ann. Surg., 1928, 88:672.

15. Herrmann, C. F.
Proc. Staff Meet., Mayo Clinic, 1928, 3:21.

16. Morton, H. B.
Surg., Gynec., & Obst., 1931, 52:1093.

17. Rice, T. B.
J. Lab. and Clin. Med., 1933, 51:381.

18. Jern, H. Z., Harvey, H. D., and Meleney, F. L.
Proc. Soc. Exper. Bact. & Med., 1932, 29:791.

19. Roberts, K., Johnson, W. W., and Bruckmer, H. S.
Surg., Gynec. & Obst., 1933, 57_752.

20. Malvoz, E.
Arch. d. Med. Exp. et d'Anat. Path., 1891, 3:593.

21. Altemeier, W. A.
Ann. Surg., 107:517, 1938.

22. Owen, C. R.
Ph.D. Thesis, University of Minnesota, June, 1939.

23. Wilkie, D. P. D.
Internatl. Clinic, 1912, 4:145.

24. Rixford, E. L.
Proc. Staff Meet. Mayo Clin., 1933, 8:586.

25. Seeley, S. F., Higgins, G. M., and Mann, F. C.
Proc. Staff. Meet. Mayo Clinic, 1935, 10:793.

26. Goldblatt quoted by Harvey and Meleney.

27. Potter, E. B., and Coller, F. A.
Ann. Surg., 1935, 102:886.

28. Coller, F. A., and Brinkman, H.
Ann. Surg., 1939, 109:942.

29. Rankin, F. W. and Bargen, J. A.
Arch. Surg., 1929, 19:906.

30. Dixon, C. F.
Surg., Gynec., & Obst., 1936, 62:770.

31. Oschner, A. and De Bakey, M.
Am. J. Surg., 1939, 46:103.

32. Rankin, F. W. and Graham, A. S.
Am. J. Surg., 1939, 46:18.

33. Trusler, H. M.
Arch. Surg., 1931, 22:983.

34. Warren, S.
Arch. Path., 1928, 6:860.

35. Vincent, H.
Compt. rend. Acad. d. Science, 1933, 197:502.

36. Weinberg, M. and Levenson, S.
Compt. rend. Soc. de biol., 1935, 118:1302.

37. Riemann, R.
Muenchen. Med. Wchnschr., 1933, 80:1886.

38. Pellegini quoted by Harvey and Meleney.

39. Perrando, G.
Zentrabl. f. Chir., 1935, 62:85.

40. Priestley, J. T. and McCormack, C.J.
Surg., Gynec. & Obst., 1933, 63:675.

41. Chiari, H. and Kunz, H.
Arch. f. Koin. Chir., 195, 181:715.

42. Pratt, J. P.
Am. J. Obst. & Gynec., 1938, 36:209.

43. Altemeier, W. A. and Jones, H. C.
J.A.M.A. 1940, 114:27.

44. Blalock, A.
Principles of Surgical Care: Shock and Other Problems.
C. V. Mosby Co., 1940, p. 287.

45. Kelly, J. F., Dowell, D. A., Russum, B. C. and Colien, F. E.
Radiology, 1938, 31:608.

46. Kelley, J. F. and Dowell, D. A.
Radiology, 1939, 32:675.

47. Des Jardins, A. U.
J.A.M.A. 1931, 96:401.

48. Bergh, G. S.
Internatl. Abst., Surg., 66:29, 1938.

IV. GOSSIP

Visitors come and visitors go bringing with them their problems some of which are difficult to solve. Here is the man who is keeping his father's ashes in a little bronze box in his room not knowing what to do with them. His secret is not shared by the other members of his family so we discuss at length possible places for disposition, including the flower beds or the lake where the departed one liked to fish....The next caller practiced hypnotism in his youth, and while a student at the University engaged in several rough and tumbling encounters with fellow students. During these fights he would lose consciousness as far as his actions were concerned. When fellow students pulled him off, he would learn that he had almost choked his opponent. We discussed this at length without getting very far....The next call was from a woman. It was a personal problem in regard to her sister and brother-in-law, which problem has apparently been discussed with the whole family. He is under treatment for lichen-planus and they wonder if the treatment has anything to do with his strange behavior....Next is the secretary of a business association who tells me with bated breath that at the meeting of the program committee they had unanimously selected me to be their speaker for a meeting which is to occur about three days off....Here is a letter from a girl who is too tall, and she wants an operation done which will shorten her legs. I can imagine that she has fallen in love with a boy scout.....The telephone rings again, and this time it is a program committee person who has decided that the radio transcription of my speech at another dinner is not going to be suitable for this dinner because someone else wants to talk....I am now up on the stage at Northrop Memorial Auditorium listening to the public program on Health Conservation sponsored by the American College of Surgeons. One of the speakers has just turned to Governor Stassen to tell him that he hopes that our Governor will be the first one to enact legislation which will limit the speed of all automobiles by placing a governor on each engine....I enjoy the story concerning the Scotchman who visited an Irish town only to be knocked down by two footpads who make for his money. After a terrible tussle, they obtain a coin which would be the equivalent of a nickel. Having done so the two thugs run for a place in the bushes to recover from their exertion. Short of breath and wiping perspiration from his face, one said to the other, "It was lucky for us it wasn't a dime he had or he would have killed us!"..It is the breakfast meeting of the Hospital Section of the American College of Surgeons Regional Meeting, and I am telling the story of training violinists. Educational psychologists tell us that to raise a violinist's ability from 40 to 60 on a scale of 100 is not as great a contribution as raising one from 90 to 92, inasmuch as perfection is the goal. After that several players worked on the same string until the last speaker changed the theme to wobbly legs on a card table. There were four of us who had spoken on the subject, and each one represented a leg...Dr. George T. Pack is now speaking at the Health Conservation Meeting, and he is building up the concept of cell division, cell differentiation, and controlled growth and comparing it with normal repair, benign and malignant tumors. He is especially lucid on the question of contagions in malignancy. In fact, this particular section of his talk is one of the best I have heard. He is the co-author of the three volumes on malignancy which represent the last word in critical analysis of our accomplishments and possibilities for the future. A new society has been formed of those interested in endocrinology. Endocrinologists tell us that we should all be endocrinologists and that we should have no department of endocrinology which seems a paradox. In each department there are several individuals interested in this subject, and a joint meeting of these persons has much to commend it. There are meetings and meetings. In fact, some persons suggest that we spend as much of our time either speaking or listening that we have little time left for thinking. In the Middle Ages before modern science came in, men grew old without benefit of glasses, store teeth, deceptive clothes, etc. They had time to sit around and become philosophers, but now we keep so busy that the ranks of the philosophers have become thin.....