It is a question whether the digitalis and nux vomica which were required for the failing heart, at a later stage of the case, may not have had an unfavourable effect, as far as the muscular wall of the intestine was concerned, increasing the spasm at the seat of stricture, and so preventing evacuation of the bowel. Possibly the increased new growth sufficed to cause complete obstruction.

V.—THE CONDITIONS INTERFERING WITH THE HEALING OF WOUNDS, WITH EXPERIMENTS ON LESION AND IMPLANTATION INFECTION.

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The healing of wounds *per primam intentionem*—the desired aim of the operative surgeon—results from a number of physiological phenomena, which together constitute the normal process of repair. In a wound running a normal aseptic course a physiological inflammation is in process, but on slight provocation this inflammation oversteps the limit of the normal physiological and becomes an abnormal pathological process.

A clear understanding of those conditions under which the processes of repair best pursue a normal course is of value, as indicating the lines upon which they can be most effectually prevented from pursuing an abnormal development.

The main condition upon which the healing of wounds by first intention depends is a state of unimpaired vitality of tissue. From the surgical standpoint, this normal tissue vitality is, broadly speaking, liable to be injuriously affected by—1, Impaired circulation; 2, Impaired nervous supply; 3, The presence of micro-organisms; 4, Mechanical irritation; 5, Chemical irritation.

That the tissues in their normal healthy state possess a vitality—a power of resistance—has been abundantly proved by experiment. So far back as 1877, Wegner[1] showed in a series of researches that the peritoneum was not so readily injured by irritants as was generally supposed. He found that great quantities of air, water, and even decomposing fluids could be injected intra-peritoneally, without consequent damage. These experiments, performed at a time when the science of bacteriology was little advanced, have since been fully confirmed by Grawitz.[2] This observer shows that it matters not "how many million cocci" are introduced into the peritoneal cavity, provided that its resorption

[1] *Chirurgische Beobachtungen über die Peritonealhöhle mit besonderer Berücksichtigung der Ovariotomie. Vortrag im V. Congress der Deutschen Chirurgischen Gesellschaft*, s. 1-77. Berlin, 1877.

[2] "Statistischer und Experimenteller Beitrag zur Kenntniss der Peritonitis," *Charité Annalen*, 1886, Bd. xi.

power is unimpaired. As soon, however, as this power is interfered with by wounds, ascites, or, in short, by anything producing a *locus minoris resistentiæ*, peritonitis ensues. Further, Fehleisen[1] injected 4-8 c. cm. of abscess pus containing staphylococcus aureus into the peritoneum of rabbits, with negative results. Again, Rinne[2] introduced 30-35 c. cm. suspension of staphylococcus aureus into the peritoneum of rabbits with negative results. Again, Rinne[2] introduced 30-35 c. cm. suspension of staphylococcus aureus into the peritoneal cavity of dogs without noticeable reaction, and even found that the administration of such enormous doses day after day produced, in the case of large dogs, no symptoms or appearances of peritonitis. Reichel[3] has injected into the peritoneal cavity 100 c. cm. fluidified gelatine culture of pus cocci with 50 c. cm. of water, without damaging the parts; while Silberschmidt,[4] in another series of experiments, proved that extremely large quantities of pyogenic organisms suspended in indifferent solutions, decomposing fluids, washings of fæces, etc., can be placed in the peritoneal cavity without danger.

These observations, although merely a small fraction of what has been done in this direction, suffice to demonstrate the very high power of resistance possessed by healthy tissues.

This normal resistant power may, however, be reduced in a marked degree by the above-mentioned injurious conditions :—

1. Impaired Circulation has been proved experimentally to exert a deleterious influence. Lingelsheim[5] found that a fresh bouillon culture of streptococcus (of which 0·1–1·0 c. cm. killed white mice in two to three days), rubbed into the slightly scarified ears of rabbits, was just sufficient to set up an erysipelas; but when the base of the ear was slightly compressed, to a degree causing no disturbance in the healthy ear, a bouillon culture, of which 0·75 c. cm. produced no effect on white mice, sufficed to produce marked erysipelas. Similarly, Waterhouse,[6] injecting staphylococcus aureus into the tissues of two persons, failed to produce abscess formation, until the parts were predisposed by constriction.

2. Impaired Nervous Supply has been shown by experiment notably to lower the resistant powers. Dache and Malvoz[7] found that $\frac{1}{3}$ c. cm. staphylococcus albus injected into normal rabbits

[1] *Von Langenbeck's Archiv*, Bd. xxxvi. s. 978.

[2] "Ueber den Eiterungesprocess und seine Metastasen," *Archiv für Klinische Chirurgie*, Bd. xxxix.

[3] "Beiträge zur Ætiologie und Chirurgischen Therapie der Septischen Peritonitis," *Habilitation's Schrift*, Leipzig, 1889.

[4] "Experimentelle Untersuchungen über die bei der Entstenung der Perforation's Peritonitis wirksamen Factoren des Darm-Inhalts," *Mittheilungen aus Kliniken und Medicinischen Instituten der Schweiz*, 1893.

[5] "Beiträge zur Streptokokkenfrage," *Zeitschrift für Hygiene*, Bd. xii. s. 317.

[6] *Experimental Researches on Peritonitis*, 1889. (Graduation Thesis.)

[7] "Nouveaux Faits concernant le rôle du Système Nerveux dans l' infection Microbienne," *Annales de l'Institut Pasteur*, 1892.

produced no local reaction; but the same quantity injected into the rump or neck of animals, whose sciatic or cervical sympathetic nerve had been divided, always led to abscess formation. It was proved that this remarkable result was not in any way connected with the immobility of the limb, as the same experiments gave similar results when repeated with uninjured rabbits, whose legs were enclosed in plaster cases. That the abscesses did not arise from faulty arterial supply was rendered apparent by ligaturing the femoral artery, when the results were negative. The same observers, in a series of experiments with the Pasteur anthrax vaccin, found that vaccin No. 1, injected into normal rabbits, produced no reaction locally; but that introduced into rabbits with divided nerves, swellings of neighbouring glands, in the form of hard nodes, supervened in two to three days. Further, vaccin No. 2, injected subsequent to No. 1, killed more than half the normal rabbits, while none died of the forty rabbits whose nerves had been divided.

3. The Presence of Micro-organisms injuriously affects the tissues, and the injury done by them varies with,—*a*, The state of the soil; *b*, their number; *c*, their virulence.

a. The State of the Soil modifies the action of organisms according to its suitability for their growth. The normal tissues are unaffected by large quantities of even virulent organisms, as shown by the experiments quoted above. Further evidence is afforded by the investigations of Ribbert.[1] He injected osteomyelitis cocci into the blood, and found them present after twenty-four hours in all the organs, but after two days they were demonstrable in the kidneys alone. On these grounds, Ribbert agrees with Virchow in his opinion that, without some local weak point, no *permanent* deposit of organisms occurs in the tissues. Kraske[2] in 1881 drew attention to the ready infection which follows operations upon diabetics, and this Roser considers to be due to the small number of organisms which undoubtedly exist even under an antiseptic dressing, sufficing in the weakened state of the tissues to infect the wound. Brieger's and Ehrlich's[3] work on mixed infection is interesting in this relation, as showing how organisms, in themselves not dangerous, can in a region whose vitality has been lowered by the action of another organism produce serious results. Rinne[4] has shown that cadaverin alone injected into animals produces non-micro-organismal suppuration. Basing his opinion on this and a number of other observations, he states that organisms act powerfully only because their toxines have reduced the normal vitality of the tissues. It has been testified by Silberschmidt,[5] in a number of experiments, that organisms injected into the peritoneal cavity

[1] "Die Schicksale der Osteomyelitiskokken," *Deutsche Medic. Wochenschrift*, 1884, s. 42.

[2] "Diabetes und Sepsis," *Centralblatt für Chirurgie*, 1881, No. 35.

[3] *Berliner Klin. Wochenschrift*, 1882, No. 42. [4] *Ibid.* [5] *Vide Supra.*

along with hard pieces of fæcal matter led invariably to fatal results, but that neither toxines, solid particles of fæces, nor micro-organisms alone suffice to produce peritonitis. When the peritoneum, however, was rendered susceptible by the action of toxines, solid particles of fæces, or other foreign bodies, the introduction of micro-organisms causes peritonitis. In this connexion it may further be mentioned that Walthard[1] has demonstrated by experiment that $\frac{1}{1000}$th part of the organisms necessary to produce peritonitis in a healthy state is sufficient to set up the condition in a peritoneum predisposed by drying.

b. Organisms vary in their Intensity of Action according to their Number.—This has been attested by abundant experimental proof. Samuel[2] in 1871 noted that 10–15 drops of pus injected into rabbits produced septicæmia, while smaller doses led merely to local suppuration. Birch-Hirschfield[3] found experimentally that when pus containing organisms was introduced under the skin of rabbits death occurred in from three to six days, the period varying with the number of organisms present in the pus. Kocher,[4] as a result of experiments dealing with the production of osteomyelitis, states that those fluids containing a larger number of organisms give rise to the condition more readily than those containing fewer. Rodet's[5] observations confirm this. Becker[6] found that small quantities of organisms from osteomyelitis injected intravenously and subcutaneously produced no reaction, while larger quantities introduced, either intravenously or intraperitoneally, caused death.

Experimental research, as well as practical observation, establish the accuracy of the opinion of Volkmann, that it matters not if one or two organisms reach a wound, but that infection only occurs when the quantity of the organisms exceeds a certain limit.

c. The Virulence of Organisms determines in a great measure their power of injury. This has been amply proved by the experiments of Ghriskey and Robb, who, in dealing with the following series of cases of wounds, handled with antiseptic precautions, found in 14 no organisms; 19, staphylococcus albus; 5, staphylococcus aureus; 6, bacillus coli communis; 3, streptococcus pyogenes; 2, streptococcus and staphylococcus albus. Where

[1] "Experimenteller Beitrag zur Kenntniss der Ætiologie der Eitrigen Peritonitis nach Laparotomie (sogen Operativperitonitis)," *Archiv für Experimentelle Pathologie und Pharmacologie*, 1892.

[2] "Die örtliche Wirkung des Eiters und der putriden Stoffe," *Centralblatt f. d. Med. Wissenschaften*, 1871, No. 20.

[3] "Untersuchungen über Pyæmie," *Archiv für Heilkunde*, 1873, Bd. xv. s. 193.

[4] "Zur Ætiologie der acuten Entzündungen," *Archiv für Klinische Chirurgie*, 1879, Bd. xxiii. s. 101–116.

[5] "De la nature de l'ostéomyélite infectieuse," *Revue de Chirurgie*, 1885, Nos. 4 et 8.

[6] "Vorl. Mittheilung über eine Arbeit welche zur Entdeckung des die acute infectiöse Osteomyelitis erzeugenden Mikro-organismus geführt hat," *Deutsche Medic. Wochenschrift*, 1883, No. 46.

staphylococcus aureus or streptococcus pyogenes were present, the wounds suppurated.

Where staphylococcus albus was found alone, the wounds healed by first intention.

Tavel's[1] numerous experiments regarding the presence of organisms in wounds running a normal aseptic course afford further illustration. He placed the glass drainage-tubes from the wounds in tubes of fluid gelatine, and examined the resulting growths. Amongst other important observations, he noted that in the antiseptic covering of antiseptically-treated wounds organisms were present in about two-thirds of the cases; that these were mostly harmless epidermis cocci; that if staphylococcus aureus was found, the wound generally suppurated; while the presence of staphylococcus albus was only exceptionally associated with wound infection.

Out of 126 cultivations from drainage-tubes, coccus epidermis albus was found thirty-one times, and infection occurred twice; staphylococcus albus was found eleven times, but no case of infection; staphylococcus aureus was found eight times—infection occurred in seven cases.

Tavel's results agree with those of Welch,[2] who noted that suppuration occurred in those wounds in which staphylococcus aureus was discovered; while the presence of staphylococcus albus in the majority of cases exercised no injurious effect on the healing process.

4. MECHANICAL IRRITATION lowers the vitality of the tissues, as is amply demonstrated by the following experiments:—

Riedel,[3] in a series of researches, undertaken to ascertain the effect of implantation of foreign bodies in the tissues, found that a 3 per cent. carbolic acid solution had no effect alone, but that when sand, meal, etc., were injected along with it, marked inflammatory signs appeared.

Silberschmidt indicates in the experiments quoted above, how solid particles in an infective fluid when injected into the peritoneal cavity determine the appearance of a peritonitis.

Walthard,[4] in his admirable contribution concerning the formation of adhesions after laparotomy, noted that in supravaginal amputation of the uterus, adhesions always formed between the serosa of the anterior uterine wall and that covering the posterior bladder wall. Considering that this adhesion formation

[1] "Die Sterilität der Antiseptisch behandelten Wunden unter dem antiseptischen Verbände," *Correspondenzblatt für Schweiz. Aerzte*, Jahrg. xxii. (1892).

[2] "Wound Infection," *International Journal of Medical Sciences*, November 1891.

[3] "Ueber das Verhälten von Blut, sowie von differenten un indifferenten Fremdkörpern in den Gelenken," *Deutsche Zeitschrift f. Chirurgie*, 1880, Bd. xii. s. 447–464.

[4] "Zur Ætiologie Peritonealer Adhæsionen nach Laparotomien und deren Verhütung," *Correspondenzblatt f. Schweiz. Aerzte*, Jahrg. xxiii., 1893.

might be due to the action of the atmospheric air upon the delicate endothelial surface, in six operations on rabbits the parts were protected by being covered with gauze kept constantly moist with a warm neutral solution. In none of these cases did adhesions form. Adhesions, however, formed when air, filtered to exclude organisms and dust particles, was allowed to exert its drying action on the peritoneal surface. This experiment excludes the possibility of the adhesions arising from an infective process. In all experiments where steam was brought in contact with an exposed peritoneum no adhesions formed. To decide whether the adhesion formation following prolonged contact with atmospheric air was due to chemical or mechanical action, oxygen, nitrogen, and carbonic acid gases were respectively brought into contact with peritoneal surfaces kept moist by steam, but in no case did adhesions form.

From these results Walthard, agreeing with Wagner[1] and Delbet,[2] concludes that even the slight mechanical irritation arising from contact of the atmospheric air with a peritoneal surface sets up a necrosis of the superficial cells—a lesion which in perfectly aseptic cases is nevertheless sufficient to lead to adhesion formation.

5. Chemical Irritation is capable of reducing the vitality of the tissues. This is admirably illustrated in the classical experiments of Councilman,[3] who in fifteen cases introduced croton oil (1 to 5 olive oil) into the subcutaneous tissues, and succeeded in each case in producing non-organismal suppuration. Further, Grawitz, de Bary, Rosenbach and Kreibohm,[4] have proved that certain chemicals in certain amounts, in certain species of animals, are capable of producing necrosis of the tissues without the presence of micro-organisms.

Wound Infection, regarded from the practical standpoint, is generally due to a combination of the three injurious conditions last mentioned, viz.,—The presence of micro-organisms; Mechanical irritation; Chemical irritation.

A publication by Kocher[5] furnishes an apt example of this combination of conditions producing an infection. In 1888, 31 major operations performed during a period of seven weeks gave only one healing *per primam*. A thorough overhauling of the antiseptic system then in use showed no possibility of infection, except through the catgut employed for ligatures, which was that prepared with juniper oil. This material was discarded and sublimate silk used in its stead. Healing by first intention was

1 *Archiv. f. Klin. Chirurgie*, Bd. xx.
2 *Centralblatt f. Chirurgie*, 1878, s. 522.
3 "Zur Ætiologie der Eiterung," *Virchow's Archiv*, 1883, Bd. xcii.
4 *Verhandlungen der Deutschen Gesellschaft für Chirurgie*, 1888.
5 "Eine Einfache Methode zur Erzielung sicherer Asepsis," *Correspondenzblatt f. Schweiz. Aerzte*, Jahrg., 1888, s. 3.

in every case obtained in the 62 operations performed after this change. Kocher ascribes his unfortunate series to an "implantation affection,"—a term by which he expresses an infection arising from organisms placed in the wound, together with some foreign material (which, in this case, were the ligatures) acting as agents lowering tissue vitality. This term of "implantation infection" is used by Kocher in contra-distinction to "contact infection," such as arises from inoculation of organisms through the medium of instruments, hands, sponges, etc.

Kocher's untoward cases, instead of depending, as he suggests, on an "implantation infection," appear to me to have been due to what I should prefer to term a "lesion infection." This I would more distinctively define as an infection of which the chief producing factor is lowered vitality of tissue, resulting from any form of external irritation. In the cases referred to, this lowered vitality was induced by the chemical irritation of the juniper oil and the mechanical irritation of the ligatures. In support of this view, I may state that juniper oil has been proved to be a very irritating chemical; while juniper oil catgut, examined bacteriologically, has never been found to contain organisms. Such organisms as were present in Kocher's infected wounds were probably of secondary importance, from the etiological standpoint. Their presence I should account for in one of two ways:—(1) They were circulating in the blood stream, and were detained at this *locus minoris resistentiæ;* or (2), they were introduced into the wound in the course of the operation, and were only capable of pyogenic action, on account of the lowered vitality induced by the catgut ligatures.

Lesion Infections, I believe, are of more frequent occurrence than has hitherto been supposed. In order to subject this view to crucial proof, and learn, if possible, the relative powers of the more common conditions which lower tissue vitality and thus permit lesion infection, I undertook the following experiments under the guidance of Herr Professor Tavel in the Bacteriological Institute at Bern, during the winter of 1893–94.

During a period of six months I made 98 inoculations on rabbits. The materials inoculated were:—Foreign bodies; Chemical irritants; Micro-organisms. Every precaution was taken to eliminate error and obtain trustworthy results. The following is a brief description of the technique of the experiments:—

The foreign bodies were knots of ordinary surgical silk of sizes 1 and 5. Large and small knots of each thickness were made up. The smaller knots consisted of about half an inch of silk doubled upon itself and tied in the middle with another piece of the same silk in a reef knot. The larger knots were made in a similar manner, but consisted of about three and a half inches of silk doubled upon itself six times. The knots thus prepared were

placed in test-tubes containing about half an inch of distilled water, and fitted with a cotton wool plug fixed midway between the water and the tube mouth, which was plugged in the usual manner. The knots were laid upon the upper surface of the lower plug. These tubes were then sterilised in compressed steam at 115° C. for fifteen minutes, and laid aside for subsequent use.

The chemical irritant employed was corrosive sublimate in solutions, the strength of 1 to 1000 of water, 1 to 100, and 1 to 20. Coloured pellets were used, dissolved in distilled water. When the silk knots were to be impregnated with any of the sublimate solutions, they were removed from the tubes with sterilised forceps, and were laid in the solution contained in sterilised glass vessels, with closely fitting glass lids, and allowed to soak. The arrival at the maximum intensity of colour was used as an indication that the knots were thoroughly impregnated with the corrosive solution.

The organisms used in the experiments were staphylococcus pyogenes aureus obtained from an acute abscess; streptococcus pyogenes from a phlegmonous erysipelas, and bacillus coli communis from abscess pus. The organisms were cultivated on agar-agar at a temperature of 37° C. Every four days new tubes were inoculated to assure a continued supply of nutrient material. The suspensions of bacteria were made by the addition of a platinum loop of culture to about 10 c. cm. distilled water, followed by thorough breaking-up of all clumps of organisms and filtration. Before using, each suspension was proved microscopically to contain organisms. The number of organisms in the single or double platinum loops used was ascertained by inoculation of gelatine afterwards poured into Petri's flat-glasses, where the developing colonies could be counted. When a knot was to be infected with such a suspension of organisms, it was removed in sterile forceps from the tube or sublimate solution, laid upon a glass slide previously sterilised by dry heat, and there, under cover of an inverted glass vessel slightly tilted, was infected by means of a platinum loop.

The preparations for the operation were as follows:—All instruments used were sterilised by boiling for twenty minutes in a 1 per cent. sodium carbonate solution, and before use were laid in a "salt soda" solution (sodium chloride 7½ per cent., sodium carb. 2½ per cent.). The glass tube and rod used directly for inoculation, as also the forceps for lifting the silk knots, were sterilised by the dry heat of a Bunsen flame.

The animals to be operated upon were tied down on their backs and an area of the skin over the abdomen, about 3 inches long by 2 inches broad, was carefully shaved; this part was next washed and brushed thoroughly with soap and water. After careful removal of the soap, sublimate 1 to 1000 was used with a nail brush, and cotton wool, previously boiled and soaked in sublimate,

applied to the part for about ten minutes. The sublimate was thoroughly washed away by the "salt soda" solution before beginning the operation. The hands were purified in the same manner as the operation area. Before cutting the skin the whole animal was covered with a cloth boiled for twenty minutes in a 1 per cent. soda solution, and afterwards soaked in the "salt soda" solution. An opening in this cloth, slightly smaller than the shaved area of skin, allowed the operation to be carried out without danger of contamination of instruments, fingers, etc., from the hair of the rabbits.

The operation was performed by making an incision through the skin and superficial fascia of the abdomen, about half an inch in length, on one or other side of the middle line and at right angles to it. A glass tube 3½ inches in length, of about ¼ inch diameter, was inserted into the incision, and pushed about 2½ inches through the subcutaneous tissues towards the groin. If foreign bodies were to be introduced, the silk knots were now placed in the entrance of the glass tube, and were pushed through it into the tissue beyond by a glass rod slightly longer than, and closely fitting, the glass tube. When organisms were to be inoculated the platinum loop was introduced through the tube. When the tissue vitality was to be lowered, the glass rod, previously heated, was passed beyond the end of the tube into the tissues, before inoculation was performed.

It will be noted that in all cases the point under observation—the site of the foreign body, etc.—was about 2½ inches from the skin wound, and the track of the glass rod and the wound itself were protected from the materials introduced, which acted alone upon the "pocket" at the farther end of the track. By sterilising the glass rod and tube by dry heat, all possibility of dilution of organismal suspensions, corrosive solutions, etc., occurring during the operation was excluded. After the inoculation was made, the tube and rod were withdrawn and the skin and fascia united by a double layer of continuous silk suture.

In some experiments, where comparatively large quantities of suspensions of organisms were introduced, a hypodermic syringe [1] was used, and the fluid injected subcutaneously, without a larger skin wound being made. In these cases the syringe was purified by boiling in 1 per cent. sodium carbonate solution and subsequent washing in "salt soda" solutions. The injections were made with an aspiration and pulsion apparatus. This consists of two glass bottles connected by an india-rubber tube. The one bottle is fixed and filled with mercury, the other is movable and can at will be placed higher or lower. In this way a chamber containing compressed or rarefied air is obtained, allowing the

[1] The syringe consisted exclusively of glass and metal, thus permitting of perfect sterilisation.

filling of the syringe, and injection into the tissues. This apparatus is advantageous, as it leaves both hands of the operator free, and the injection takes place regularly without jerks.

The inoculations comprised in each series of experiments were always performed upon the same day, with as short an intervening interval as possible, in order that during subsequent observation true comparisons might be obtained.

After an inoculation was performed, the rabbits were returned to the hutches and kept under observation until any appearances of inflammatory action had subsided. Each animal was visited twice in the twenty-four hours, and careful record made of the state of the parts. By this means the time of the appearance and disappearance of swelling in the case of simple inoculations could be determined within twenty-four hours, while after the introduction of the knots, the ease with which the separate threads could be felt enabled a decision to be arrived at as to the presence or absence of inflammatory thickening. The animals remained under observation, according to circumstances, for periods ranging from seven to forty days.

Where organisms were introduced, suppuration in the skin wound, or in the track along which the glass tube had been passed, was by no means easy to prevent, even with the precautions used. The individual experiments in which such an infection occurred being obviously useless, it was necessary for comparative purposes to repeat the whole series.

In the following pages I have tabulated 78 experiments. I have not included 20 experiments belonging to those series in which a suppuration in the track of inoculation occurred, and which were repeated.

In the tables, I have used the term "reaction" to indicate any visible hyperæmia or swelling noticeable on inspection or palpation.

TABLE A shows experiments illustrating the effects of foreign bodies introduced, and indicates that reaction, as previously defined, lasts longer when such foreign bodies are present than when none are present, and that the larger the foreign body the greater is the reaction and the longer its duration.

The practical deductions to be drawn from the above results are,—that as little ligaturing material as possible should be employed in wound treatment. Instead of ligaturing, other methods of arresting hæmorrhage, such as torsion and forcipressure, etc., should be used as much as possible. Further, the ligature material employed should be absorbable, in order that it may, in a comparatively short time, cease to be a foreign body. Hence catgut should be used rather than silk.

TABLE B shows the effect of foreign bodies introduced along with a chemical irritant, and from these experiments it is seen that the use of corrosive sublimate, even in a dilution of 1–1000, was sufficient to increase the amount and duration of the reaction set up by the foreign substance, and, further, that the reaction increased *pari passu* with the strength of the sublimate solution.

On this ground, then, the wounded tissues should be protected from the action of strong antiseptics, and nothing but "indifferent" solutions should be permitted to come in contact with them. Thus, before beginning an operation, strong antiseptics previously employed for cleansing the parts should be washed away by some solution which has no injurious effect on the tissues, and during the operation such a solution should alone be used. Suitable for such purposes are boiled water, "normal salt" solution, or the "salt soda" solution consisting of 2½ per cent. common salt and 7½ per cent. sodium carbonate, recommended by Prof. Tavel, and now generally used in Germany and Switzerland.

TABLES C, D, E, exemplify that—The action of micro-organisms depends upon the number introduced.

C, D, E, No. 1, show that—A large number of organisms produce abscess formation.

C, D, E, No. 2, show that—A lesser number cause swelling and hyperæmia.

C, D, E, No. 3, show that—Minute inoculations give no reaction.

These facts are illustrated in the case of—

Staphylococcus aureus in the series		C, *a*, 1, 2, and 3.
For streptococcus pyogenes	„	D, *a*, 1, 2, and 3.
For bacterium coli communi	„	E, *a*, 1, 2, and 3.

It may, therefore, be concluded that such few organisms as undoubtedly gain entrance to wounds through the air or from other sources, even under the strictest antiseptic precautions, are not to be dreaded, provided the tissues are maintained as far as possible in their normal state of vitality. Volkman's view is corroborated, that it is only when a certain moderate quantity of organisms is exceeded that an infection is produced.

SECTIONS *b*, 1, in each of the Tables C, D, E, show how a number of organisms, which the experiments in *a*, No. 3, demonstrate to have been harmless in healthy tissues, give rise, when the tissues are in a state of lowered vitality, to a marked reaction, producing, in fact, a "lesion infection."

These striking results enforce avoidance of all forms of mechanical irritation. As has been also inculcated by the previous experiments, the surgeon should use only indispensable ligatures and the most neutral and indifferent of solutions. While

particular attention should be paid to the avoidance of that form of irritation caused by drying of the parts during operation, Walthard, as before mentioned, has shown that such drying of peritoneal surfaces is sufficient to set up a necrosis of the superficial cells determining adhesion formation.

Sections *b*, 2, in Tables C, D, E, show a number of organisms (which even in tissues of lowered vitality were unable to produce a reaction) enabled to do so by the addition of the devitalizing action of a foreign body, constituting an "implantation infection."

Hence is again enforced the importance that foreign bodies shall not be introduced into wounds.

Tables F, G, H, show—*First*, a series of bacterial inoculations with a quantity of the suspension, which was insufficient to cause a reaction even in the injured tissues; *second*, a series of experiments where the same quantity of bacterial suspension in conjunction with the presence of a foreign body set up marked inflammatory action. *Finally*, the last set of observations show the organisms unable to take advantage of the irritation produced by the knots on account of the bactericidal power of the sublimate present; with the noteworthy result that the reaction produced was only *equal* to that which appeared when the knots and sublimate were introduced without any organisms at all.

Since ligatures thus predispose to infection, the practical inference is, that they should be impregnated with some mild antiseptic. It is not enough to have the ligature material aseptic or indifferent; it should be antibacterial.

I consider that these experiments, comprising nearly 100 inoculations, afford some measure of the relative powers of the several conditions which interfere with the normal healing of wounds. They demonstrate the injurious effects of mechanical and chemical irritants in lowering tissue vitality. And they illustrate how the *locus minoris resistentiæ* thus produced permits a lesion infection to be established by organisms in such moderate numbers and of such slight virulence as are proved to be harmless in healthy tissues. They thus enforce the careful protection of wounds during operation from every condition which is liable to impair normal physiological vitality, and interfere with the subsequent healing process.

TABLE A.

CONTROL EXPERIMENT.—*To estimate the reaction resulting from the irritation of the operation alone.*

Operation performed, glass tube inserted, and withdrawn without introduction of any foreign material			Reaction during 36 hours.
Introduction of knots sterilised with compressed steam at 115° C. for 15 minutes	Size 1	Small knot	„ „ 5 days.
		Large „	„ „ 10 days.
	Size 5	Small „	„ „ 10 days.
		Large „	„ „ 13 days.

TABLE B.

(1.) Introduction of knots sterilised by compressed steam at 115° C. for 15 minutes, plus sublimate 1-1000	Size 1	Small knot	Reaction during 12 days.
		Large „	„ „ 13 days.
	Size 5	Small „	„ „ 12 days.
		Large „	„ „ 20 days.
(2.) Introduction of knots sterilised by compressed steam at 115° C. for 15 minutes, plus sublimate 1-1000	Size 1	Small „	„ „ 12 days.
		Large „	„ „ 20 days.
	Size 5	Small „	„ „ 18 days.
		Large „	Reaction marked; on the 10th day the animal died. *Sectio* showed wound perfectly healed; no trace of pus; no pus about knot; no colonies developed in tubes inoculated from these parts; abscesses in liver containing staphylococci; staphylococci present in blood; other organs healthy.
(3.) Introduction of knots sterilised by compressed steam at 115° C. for 15 minutes, plus sublimate 1-20	Size 1	Small knot	Reaction marked; remained during 32 days.
		Large „	Reaction marked; animal died on 8th day. *Sectio*—Wound healed; no pus or organisms about knot; liver abscesses with staphylococci—none in other organs or blood.
	Size 5	Small „	Reaction very marked; lasted 30 days.
		Large „	Reaction very marked; animal died on 5th day. *Sectio*—Wound healed; no pus about knot; no organisms could be cultivated; organs healthy; staphylococci in blood.

TABLE C.

a. VITALITY OF TISSUES UNIMPAIRED.

(1.) *Pure Culture Staphylococcus Aureus.*

Introduction of—

0·6 c. mm	Abscess.
0·6 c. mm. pure culture + small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.) . . .	Abscess.
0·6 c. mm. pure culture + large knot (Size 5, sterilised by compressed steam at 115° C. for 15 min.) . . .	Abscess.

(2.) *Suspension Staphylococcus Aureus*—250 colonies in small platinum loop (0·6 c. mm.)

Introduction of—

1 c. cm. suspension	Reaction during 10 days ; no abscess.	
0·1 c. cm. „ + 0·9 Aq. dest.	No reaction.	
0·0006 c. cm. „ + 1 c. cm. Aq. dest.	No reaction.	
0·0006 c. cm. „ + small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.) . .	Reaction during 5 days.	Same as sterile knots, Table A.
0·0006 c. cm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min)	Reaction during 10 days.	

(3.) *Suspension of Staphylococcus Aureus*—1400 colonies in double platinum loop (4·0 c. mm.)

Introduction of—

4·0 c. mm. suspension	No reaction.	
4·0 c. mm. „ + large knot (No. 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 11 days.	Same as sterile knot, Table A.

b. CONTROL EXPERIMENT.—*To estimate the reaction resulting from the irritation of the operation in tissues of lowered vitality.*

Operation performed ; glass tube inserted ; tissue vitality lowered by burning with hot glass rod ; no introduction of foreign material, . .	Reaction during 3 days.

b. VITALITY OF TISSUES IMPAIRED (BURNING WITH HOT GLASS ROD).

(1.) *Suspension of Staphylococcus Aureus*—900 colonies in double platinum loop (4·0 c. mm.).

Introduction of—

4·0 c. mm. suspension	Reaction during 5 days.	Compare C, *a*, (3).
4 0 c. mm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 18 days.	

(2.) *Suspension of Staphylococcus Aureus*—460 colonies in small loop (0·6 c. mm.).

Introduction of—

0·6 c. mm.	Reaction 3 days (as in Control Experiment—burning alone).
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 17 days.

TABLE D.

a. Vitality of Tissues Unimpaired.

(1.) *Pure Culture Streptococcus.*
Introduction of—

0·6 c. mm.	Abscess.	
0·6 c. mm. + small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Abscess.	
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Abscess.	

(2.) *Suspension of Streptococcus*—650 colonies in small platinum loop (0·6 c. mm.).
Introduction of—

1·0 c. cm. suspension	Reaction moderately strong, lasting for 7 days; no abscess.	
0·1 c. cm. „	No reaction.	
0·0006 c. cm. „	No reaction.	
0·0006 c. cm. + small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 5 days.	Same as sterile knots, Table A.
0·0006 c. cm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 11 days.	Same as sterile knots, Table A.

(3.) *Suspension of Streptococcus*—2250 in double platinum loop (4·0 c. mm.).
Introduction of—

4·0 c. mm. suspension	No reaction.	
4·0 c. mm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 10 days.	Same as sterile knot, Table A.

b. Vitality of Tissues Impaired (Burning with Hot Glass Rod).

(1.) *Suspension of Streptococcus*—1990 colonies in double loop (4·0 c. mm.).
Introduction of—

4·0 c. mm. suspension	Reaction during 8 days.	Compare D, *a* (3).
4·0 c. mm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 17 days.	Compare D, *a* (3).

(2.) *Suspension of Streptococcus*—800 colonies in small loop (0·6 c. mm.).
Introduction of—

0·6 c. mm. suspension	Reaction during 3 days (as in Control Experiment with burning alone).
0·6 c. mm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 23 days.

TABLE E.

a.—Vitality of Tissues Unimpaired.

(1.) *Pure Culture Bacterium Coli Commune.*

Introduction of—

0·6 c. mm.	Abscess.
0·6 c. mm. + small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Abscess.
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Abscess.

(2.) *Suspension of Bacterium Coli Commune*—5200 colonies in small platinum loop (0·6 c. mm.).

Introduction of—

1 c. cm. suspension		Reaction marked; lasted 18 days; no abscess.
0·1 c. cm. „	+ 0·9 c. cm. dist. water	No reaction.
0·0006 c. cm. „	+ 1·0 c. cm. „ „	No reaction.
0·0006 c. cm. „	+ small knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 4 days.
0·0006 c. cm. „	+ large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 10 days.

Same as sterile knots, Table A.

(3.) *Suspension of Bacterium Coli Commune*—10,500 colonies in double loop (4·0 cm).

Introduction of—

4·0 c. mm. suspension		No reaction.
4·0 c. mm. „	+ large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 10 days. Same as sterile knot, Table A.

b.—Vitality of Tissues Impaired (Burning with Hot Glass Rod).

(1.) *Suspension of Bacterium Coli Commune*—8600 colonies in large loop (4·0 cm.).

Introduction of—

4·0 c. mm. suspension		Reaction during 9 days.
4·0 c. mm. „	+ large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 27 days.

(2.) *Suspension of Bacterium Coli Commune*—2200 colonies in small loop (0·6 c. m.).

Introduction of—

0·6 c. mm. suspension		Reaction during 5 days.
0·6 c. mm. „	+ large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.),	Reaction during 20 days.

(3.) *Suspension of Bacterium Coli Commune*—4500 colonies in small loop (0·6 cm.).

Introduction of—

0·6 c. mm. suspension		Reaction 3 days (as with burning alone).
0·6 c. mm. „	+ large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 24 days.

TABLE F.

CONTROL EXPERIMENT.

To estimate the reaction resulting from the irritation of the operation when a large knot (Size 1), sterilised by compressed steam at 115° C. for 15 minutes and by sublimate 1-1000, was introduced into tissues of lowered vitality . . . Reaction during 18 days.

VITALITY OF TISSUES IMPAIRED (BURNING WITH HOT GLASS ROD).

Suspension of Staphylococcus aureus—420 colonies in small loop (0·6 c. mm.).

Introduction of—

0·6 c. mm.	Reaction during 3 days (as in Control Experiment with burning alone).
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 minutes)	Reaction during 20 days.
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 minutes, and by sublimate 1-1000)	Reaction during 18 days (same as Control Experiment *supra*).

TABLE G.

VITALITY OF TISSUES IMPAIRED (BURNING WITH HOT GLASS ROD).

Suspension of Streptococcus—750 colonies in small loop (0·6 c. mm.)

Introduction of—

0·6 c. mm. suspension	Reaction 3 days (as in Control Experiment with burning alone).
0·6 c. mm. „ + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min.)	Reaction during 22 days.
0·6 c. mm. „ + large knot (Size 1, sterilised by steam and by sublimate 1-1000)	Reaction during 19 days (similar to Control Experiment, Table F).

This series of experiments required to be repeated three times—as with suspensions of streptococcus containing respectively 1600 and 2000 colonies in a small loop, reaction was noted when 0·6 c. mm. was introduced alone. Also in these cases the reaction produced by the infected sublimate knot was greater than that observed in the Control Experiment, where a sterile sublimate knot was introduced into the damaged tissues.

TABLE H.

VITALITY OF TISSUES IMPAIRED (BURNING WITH HOT GLASS ROD).

Suspension of Bacterium Coli Commune—3000 colonies in small loop (0·6 c. mm.).

Introduction of—

0·6 c. mm.	Reaction 3 days (as in Control Experiment with burning only).
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 113° C. for 15 min.)	Reaction during 21 days.
0·6 c. mm. + large knot (Size 1, sterilised by compressed steam at 115° C. for 15 min., and sublimate 1-1000)	Reaction during 17 days (same as Control Experiment, Table F).