Lecture.

MORBID CONDITIONS CAUSED BY BACILLUS AÉROGENES CAPSULATUS.¹

THE SHATTUCK LECTURE.

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MR. PRESIDENT AND FELLOWS OF THE MASSACHUSETTS MEDICAL SOCIETY:—Although the subject which I have chosen for this lecture relates for the most part to infrequent affections, the scientific and practical interest attaching to them is considerable and varied. Many instances of the presence of free gas in parts of the body where it does not normally occur and in association with various diseases were recorded by writers of past centuries and were even then the subject of much speculation. The discussion turned generally around the question whether the gas was atmospheric air or the result of putrefaction—a question which in most cases could be solved only by bacteriological examinations. The most numerous and important of such examinations have been made during the last decade, and, although these have left problems still unsolved, they have corrected many current errors and have shed a flood of light upon conditions which were formerly among the most mysterious in pathology.

While it has been demonstrated that various bacteria may be concerned in producing gaseous affections, it is now evident that the bacillus which I discovered in 1891, and to which I gave the name *Bacillus aerogenes capsulatus*, is the one whose causative agency is best established and most frequently in action. What I shall say will relate mainly to this micro-organism and its pathogenic effects.

Historical.—As a certain amount of confusion concerning the dates of the first publications² on this bacillus exists in foreign literature on this subject, it may be well to state that I reported my observations in November, 1891, to the Johns Hopkins Hospital Medical Society and that the full report of these observations and of the characters of the bacillus was published in July-August, 1892, by Dr. Nuttall and myself.³ E. Fraenkel's first publication⁴ was a short preliminary one which appeared in January, 1893, and was followed in the same year by his valuable monograph on gaseous phlegmons.⁵ In August, 1893, one year after the publication of the paper by Nuttall and myself, appeared simultaneously the interesting articles of P. Ernst⁶ and of Graham, Steward and Baldwin.⁷ Early in 1894, Mann published from my laboratory an observation of emphysematous gangrene caused by *Bacillus aerogenes capsulatus*⁸ and in January, 1896, Dr. Flexner and I published an extensive paper reporting 23 human cases, including not only 6 personal observations of emphysematous gangrene but also examples of submucous gas cysts, pneumoserositis, and various other pathogenic mani-

festations of this bacillus.⁹ In July, 1895, appeared Goebel's preliminary communication¹⁰ and in the following year his full paper on foamy organs.¹¹ Of the subsequent records the most numerous and valuable have appeared in this country, although they appear to be little known to most European writers.¹² I shall have occasion to refer later to many of these publications.

Nomenclature.—Dr. Fraenkel has kindly favored me with cultures of the bacillus which he cultivated from gaseous phlegmons and to which he gave the name "*Bacillus phlegmones emphysematosæ*." There can be no question whatever as to the identity of his bacillus with our *Bacillus aerogenes capsulatus*, a point upon which we are both agreed, and which is also made certain by Goebel's studies under Fraenkel's supervision. According to the generally accepted principles of the nomenclature of zoological and botanical species, the latter name, as being the first one applied, should be preferred to the former. It is, moreover, as pointed out by Muscatello, not open to the objection of implying exclusive relationship to a single disease, as is the case with Fraenkel's designation of the bacillus. As a matter of fact, the capacity to produce gaseous phlegmons is only one of many pathogenic manifestations of *Bacillus aerogenes capsulatus*. Unfortunately I think that we both erred against the canons of botanical nomenclature in using a trinomial rather than a binomial name for a species.¹³

Characters of bacillus.—Since our first publication only one material addition has been made to the extended description given by Nuttall and myself of the morphological and cultural characters of *Bacillus aerogenes capsulatus*, or the gas bacillus, as I shall briefly call it.¹⁴ Fraenkel noted the presence of spores in a few of the bacilli growing in one lot of agar containing sodium formate and in 1897, Dunham¹⁵ observed spores in blood-serum cultures, but not in other media.

Our further studies of the gas bacillus obtained from different sources have shown a moderate range of variation in some of its properties. This is true especially of spore formation, rapidity of liquefaction of gelatine, presence of capsules, retention of Gram's stain, and virulence. While some specimens of the

¹ Journal of Experimental Medicine, 1896, i, p. 5.

² Centrabl. f. allg. Path. u. path. Anat., vi, p. 405.

³ Jahrb. d. Hamburg. Staatskrankenanstalt, iv.

⁴ Thus v. Hübner in 1890 (Centrabl. f. Bakt. xxv, p. 513, et seq.) in an elaborate study of pathogenic anaerobes is entirely ignorant of our work and that of other American investigators on *Bacillus aerogenes capsulatus*. The information of Hirschmann and Lindenthal (Sitzungsber. d. k. Akad. d. Wiss., Math.-Naturw. Cl., Wien, 1899) on the American work is second-hand and both incomplete and inaccurate, in these respects being in unfavorable contrast to that of Muscatello and Gangitano (Riforma Med., 1900, ii, p. 508, et seq.) writing also on the subject of emphysematous gangrene. Knowledge of *Bacillus aerogenes capsulatus*, under the name "*Bacillus porfirigenus*," has begun to appear in France in the last two years, but without any evidence of acquaintance with the American publications. Even allowing for the great difficulties in keeping pace with the literature of any subject in medicine, a decade would certainly seem sufficient for the light to penetrate even into dark places.

⁵ Migula, who, with considerable success, has attempted to reform bacteriological nomenclature, has given the binomial names "*Bacterium Welchii*" to *Bacillus aerogenes capsulatus* and "*Bacterium emphysematosum*" to *Bacillus phlegmones emphysematosæ* (System der Bakterien, ii, pp. 392 and 393, Jena, 1900). He is, however, in error in describing this organism under two different names, as his *Bacterium Welchii* and *Bacterium emphysematosum* are identical.

⁶ As regards these characters, it will suffice here to say that the micro-organism is a rather coarse, non-motile anaerobic bacillus staining by Gram, growing on all of the ordinary culture media under anaerobic conditions, best at body temperature, but also at room temperature, forming spores inconstantly, according to the race and the culture medium, and capable of forming gas not only by fermentation of sugars but also from proteids. The full description of the characters may be found in Welch and Nuttall's paper. The gas, according to Dunham's analyses, is composed approximately of 64% hydrogen, 28% carbon dioxide and 8% of a residual gas believed to be mainly nitrogen. It has no foul odor.

⁷ Bulletin of the Johns Hopkins Hospital, 1897, viii, p. 68.

¹ Delivered before the Massachusetts Medical Society, June 12, 1900.

² Levy's description in 1891 (Deutsche Zeit. f. Chirurg., xxxii.) of "kleine, feine" bacilli, cultivated from a gaseous abscess and growing in long threads and chains only at body temperature and cultivable only in the first generation, without animal experiments, cannot be accepted as an identification of *Bacillus aerogenes capsulatus*, or indeed be readily reconciled with its characters.

³ Bulletin of the Johns Hopkins Hospital, 1892, iii, p. 81.

⁴ Centrabl. f. Bakt., xiii, p. 13.

⁵ Ueber Gasphlegmonen, Hamburg u. Leipzig, 1893.

⁶ Virchow's Archiv., cxxxiii, p. 308.

⁷ Columbus Medical Journal, xii, p. 55.

⁸ Annals of Surgery, xix, p. 187.

bacillus seem never to form spores on any culture medium, others, and these appear to be the more common, do so occasionally, especially upon blood-serum, in mannite bouillon, and on plain agar. In animals inoculated with pure cultures we have not observed spore-bearing bacilli.

As a rule the bacillus liquefies gelatine slowly, but some specimens do so scarcely at all, and others with fair rapidity.¹⁶

As stated in our original articles, capsules are not constantly present, but I have generally found no difficulty in demonstrating them in the situations and by the method described by us, and, with the exception of Hirschmann and Lindenthal, most other investigators have been able to demonstrate capsules when these are searched for by suitable methods.

While the bacillus is to be ranked among those which stain by Gram, it is sometimes rather noticeable in cover-slips from cultures that among well stained bacilli others are partly or wholly decolorized, and this may be observed in members of a single chain. In the tissues the bacilli stain well by Gram. Differences in the viability of cultures were pointed out in our first paper.

It sometimes happens that original cultures from human beings show only a feeble growth, with relatively weak power of gas production, while subsequent cultures, especially those obtained after passage through the animal body, present the usual vigorous growth and other typical characters. Pratt and Fulton¹⁷ from a typical case of foamy organs with gas throughout the body were unable to cultivate the bacillus at all, although twelve anaerobic culture tubes containing various media were inoculated from different parts of the body. This negative result they attribute to the fact that the body had lain in a cold-storage vault for sixteen hours after death, an explanation which has some support in an observation previously reported by Welch and Flexner, but still seems hardly satisfactory, as under similar conditions the bacillus has been often cultivated.

Lactose, glucose and saccharose are all fermented by the gas bacillus, the first with the largest production of gas and the last with the smallest. There is apparently no fermentation of mannite, at least the gas is not appreciably more than in sugar-free media. The amount of hydrogen greatly preponderates over that of carbon dioxide.

E. Fraenkel, in 1893, was the first to demonstrate the etiological relation of the gas bacillus to gaseous phlegmons, our previous investigations being concerned mainly with the so-called foamy organs (Schaumorgane) and the presence of gas in the blood, our results being confirmed a year later by P. Ernst. Soon after Fraenkel's publication we were able to confirm his discovery of the causation of gaseous phlegmons by *Bacillus aerogenes capsulatus*, and to repeat with like results his animal experiments.

Material or cultures fresh from the infected body are usually highly virulent for guinea pigs, pigeons and sparrows (E. Fraenkel), which succumb to a rapidly spreading local necrosis of the tissues with abundant development of gas, the bacilli invading the blood during life only in small number or not at

all. There is more or less bloody edema, but otherwise little inflammatory reaction, leucocytes being present usually only in small numbers in the exudate. Rabbits and mice, while not wholly immune, are far less susceptible than guinea pigs and pigeons. Dr. Lanier, in my laboratory in 1896, succeeded in producing typical gaseous phlegmons around the fractured bones of rabbits inoculated intravenously with pure cultures, and Muscatello has obtained the same results. Welch and Nuttall reported an instance of death of a pregnant rabbit after intravenous inoculation, the infection with the gas bacillus originating in a dead fetus. There are considerable differences in the degree of virulence of the bacillus, even in fresh cultures, and old ones may be of slight virulence.

One of the most interesting and valuable tests of the gas bacillus is its power of producing gas abundantly in the blood, organs and tissues of rabbits killed a few minutes after intravenous injection, a power not possessed by colon bacilli. The differential value of this test is as great as that of cultures in fermentation tubes. The blood and tissues of the dead rabbit make the culture medium, the body of the animal takes the place of the test tube, the inoculation is an aseptic one, the bacteria are spread by the blood-current and the conditions are anaerobic. This procedure, which was introduced by Nuttall and myself and has been fully described by us, we have found useful in isolating the bacillus, in separating it from other bacteria which may resemble it, and in the demonstration of one of its most fundamental characteristics, namely, the power to produce gas from proteid material.

Among the points distinguishing the bacillus of malignant edema from *Bacillus aerogenes capsulatus* may be mentioned the following: The malignant edema bacillus is somewhat thinner, has greater tendency to grow into filaments, is less readily stained by Gram, produces spores regularly in culture media, is motile, liquefies gelatine more rapidly, produces a foul odor, produces less gas in lactose bouillon, peptonizes clotting casein, generates little or no gas in rabbits inoculated intravenously and then killed, and by subcutaneous inoculation in susceptible animals causes spreading bloody edema with little or no development of gas bubbles, and appears after death in filaments on serous surfaces.

The bacillus to which Lindenthal¹⁸ has quite unnecessarily given the name *Bacillus emphysematis vaginae* is doubtless identical with *Bacillus aerogenes capsulatus*. The same is true of Veillon and Zuber's¹⁹ *Bacillus perfringens* found by them in appendicitis, by Guillemot^{19a} in gaseous gangrene, and by Soupault and Guillemot^{19b} in gaseous abscesses, and of Buday's²⁰ *Bacillus cadaveris butyricus*, found in foamy organs. I am strongly inclined to the opinion that the anaerobic bacillus isolated by Achaïne and others from several cases of acute articular rheumatism and found by Savtchenko and Mielkitch in the soil is likewise identical with our gas bacillus.²¹

Distribution.—The surmise expressed by Welch and Nuttall that the gas bacillus is widely distributed in nature has since been confirmed. The natural habi-

¹⁶ *Wien. klin. Woch.*, 1897, p. 3, et seq.

¹⁷ *Arch. de méd. exp.*, 1898, x, p. 539.

¹⁸ *Compt. rend. Soc. de Biol.*, 1898, 10, s. v. p. 1017.

¹⁹ *Bull. et. mém. Soc. méd. d. hôp. de Paris*, 1900, 3, s., xvii, p. 216.

^{19a} *Contralbl. f. Bakt.*, 1898, xxiv, p. 309.

^{19b} *Achaïne: Ann. de l'Inst. Pasteur*, 1897, xi, p. 845; *Pic and Lesieur: Jour. de phys. et de path. gén.*, 1899, i, p. 1007, and *Savtchenko and Mielkitch: Arch. russes de path.*, 1899, viii, p. 145.

¹⁶ In our original communication we noted peptonization and softening of the gelatine, but this was so slow and slight with the particular specimen studied that we then preferred to class the bacillus among the non-liquefiers. Further experience has shown that the bacillus is a liquefier, but generally a slow one.

¹⁷ *Boston Medical and Surgical Journal*, June 7, 1900, p. 599.

tat of the organism is the intestinal canal and the soil, the home of so many other anaerobic bacteria. Welch and Flexner in 1896 brought evidence of the presence of the bacillus in both of the situations mentioned. Clopton, of the Johns Hopkins Hospital, has found the bacillus twice in the appendix vermiformis. Howard²² has recently reported the presence of morphologically identical bacilli in the intestines of 25 consecutive human cases examined post mortem, and in 10 of these he demonstrated the bacillus by cultures and inoculation of animals. The same conclusion has been reached by Hirschmann and Lindenthal. The gas bacillus has been repeatedly cultivated from the intestine in my laboratory, but we have made no systematic study of the frequency of its presence. I have found the bacillus also in the intestines of rabbits, dogs and swine, and here it is interesting to note the frequency with which submucous gaseous blebs are found in the pig's intestine at autopsy.

In 1896 Dr. Walker at the Johns Hopkins Hospital succeeded in finding the gas bacillus in dust collected by sweeping floors, proving its presence both by cultures and animal experiments. My assistant, Dr. Harris, has cultivated the bacillus from the contents of an old cesspool. I had previously reported in 1896 the isolation of the bacillus from a bullet removed from the head of the tibia in a case of gaseous phlegmon, and E. Fraenkel²³ has cultivated the gas bacillus from a splinter of wood extracted from a wound in a case of tetanus. These observations confirm the natural inference to be drawn from the study of cases of traumatic emphysematous gangrene, in most of which the source of infection is manifestly foreign material, especially dirt, in wounds. In the light of these demonstrations of the wide distribution of the gas bacillus in the outer world and in feces, the conclusion is warranted that it must occasionally be present upon the human skin.

We are not informed whether there are differences in the regional distribution of the gas bacillus. The fact that during the last decade a larger number of cases of emphysematous gangrene have been reported from Baltimore than from any other single locality is due probably to our interest in the subject and consequent search for cases. The bacillus has been found not only in America and Europe, but Dr. Flexner has brought back reports of three infections with the gas bacillus in Manila observed during a stay of three months.

GAS BUBBLES IN THE BLOOD AND ORGANS.

We turn now to the consideration of the various conditions in which the gas bacillus has been found in human beings. We need not pause to consider the presence of this bacillus in ordinary cadaveric decomposition, a circumstance sufficiently explicable by the occurrence of this organism in the healthy intestinal canal.

Of an entirely different nature are the cases in which gas bubbles are found in the blood and organs within a few hours after death and without any trace of ordinary putrefaction. Such a condition has been recognized at autopsies as soon as one, two, three, five, eight hours after death. It may occur not only after death from gaseous phlegmon, when, however,

it is by no means constant, but also after death from the most varied causes. It has been observed repeatedly in autopsies on pregnant and puerperal women, especially after death from abortion, operation for placenta previa and acute sepsis. There is every gradation from cases with a few bubbles of gas in the blood or tissues to those with extensive emphysema of the organs and tissues. The term "foamy organs" (Schaumorgane of the Germans) may be applied to the latter condition. The liver is the organ most frequently the seat of early and abundant development of gas, but there is no definite rule as to the distribution and amount of gas in different cases. As will be explained later, the invasion in the majority of cases is from the intestine. That the gas bubbles may be dislocated from their original position in liquid and soft material in the body is self evident, but I have not found them unassociated with gas bacilli.

Formerly this early presence of free gas in the heart and vessels, without evident post-mortem decomposition, was very generally explained by the assumption of entrance of air into the circulation, even when no portal of entry could be found.²⁴ The most extensive application of this explanation was made in the pregnant and puerperal cases. It is remarkable that the first case of this nature to be examined bacteriologically was that reported by me in 1891. In this and in all subsequent similar cases with satisfactory bacteriological examination *Bacillus aerogenes capsulatus* was found.

The main questions which arise concerning the interpretation of these cases are whether the invasion of the bacilli and whether the development of the gas are ante-mortem or post-mortem phenomena.

Rabbits survive the introduction of large numbers of gas bacilli directly into the circulation, unless there exists somewhere in the body necrotic or damaged tissue offering little or no vital resistance. If the animal be killed within a few minutes after the intravenous injection of the bacilli and kept in a warm place there are abundant multiplication of the bacilli and large development of gas throughout the dead body within the space of six or eight hours; whereas if the bacilli be introduced at one point, as for example the right heart, of a rabbit just killed, it takes a much longer time, often twenty-four to forty-eight hours, for gas and bacilli to make their appearance at points far distant from the seat of inoculation. It seems justifiable to draw from these three groups of experiments, which have been fully reported by Welch and Nuttall, the conclusion that when bacilli and gas are found within a few hours after death widely distributed in the body, the gas bacilli have entered the circulation during life, but probably in most cases only shortly before death.

There is one factor, however, to be considered which is absent in the experimental cases and may be present in human beings, to wit, the quick disappearance of the bactericidal power of the blood. This factor is an important determinant of the rapidity of onset of post-mortem decomposition. After death from certain diseases, and particularly from snake venom, bacteria may make their appearance in the blood and organs very soon after death. An explanation of these cases is furnished by the experiments of Ewing and myself,²⁵ which demonstrated that the blood of rabbits

²² Contributions to the Science of Medicine, dedicated by his Pupils to William Henry Welch on the Twenty-fifth Anniversary of his Doctorate, p. 461, Baltimore, 1900.

²³ Münch. med. Woch., 1899, Nos. 42 and 43.

²⁴ Closs: Luft im Blute, Stuttgart, 1854, and Couty: Thèse de Paris, 1875.

²⁵ Lancet, 1894, i, p. 1236.

killed by rattlesnake venom is practically devoid of bactericidal power, so that immediately after or even shortly before death bacteria can start growing in the body as they would in a tube of beef broth. But after all due allowance has been made for the possible reduction or loss of bactericidal power of the blood, I still consider that it is not possible to explain some of the cases in which bacilli and gas have been found in the heart, blood-vessels and organs very soon after death, especially when the corpse has been kept in a cold place, otherwise than upon the assumption of the distribution of the bacilli by the circulating blood.

It is another question whether gas as well as bacilli may be present in the circulating blood and internal organs during life in the class of cases now under consideration, and I regret to be unable to furnish a positive answer to this question. I do not see how an affirmative answer can be obtained otherwise than by the actual demonstration of gas in these situations either during life or immediately after death. Gas bubbles and bacilli have been found in the heart and vessels within an hour after death, but that is time enough for bacilli which have already been introduced to multiply and begin to form gas. I at first thought that absence of nuclear staining around the gas bubbles and masses of bacilli might serve as an indication of their presence during life, and this view is advocated by P. Ernst, but I have since learned from experiments on rabbits that this is not a decisive criterion, although often both in rabbits and human beings there is no defect in nuclear staining around bacilli and gas bubbles.

I know of no other pathogenic micro-organism which offers such difficulties in determining whether its effects in the interior of the body have been produced before or after death. The difficulty arises from the circumstance that these effects in most cases and most situations consist almost entirely in local necrosis and formation of gas, whether the invasion and growth of the bacilli be before or after death, and that unlike most pathogenic bacteria the gas bacillus grows better in the dead than the living body. Possibly some importance in the solution of the problem may attach to the demonstration of emboli of liver cells and of bone-marrow cells, which were in enormous numbers in the pulmonary vessels in a case of gaseous phlegmon of the submammary tissues following infusion of salt solution. At the autopsy made by Dr. Carroll the liver and other organs were emphysematous. Further observations with reference to these emboli in this class of cases are needed.

I do not consider that there is any inherent improbability in the supposition that gas bubbles may be in the circulating blood during life without causing speedy death from gaseous embolism. It is only when a large volume of air is introduced quickly into the blood-current that sudden death results from air embolism. Very exaggerated ideas have prevailed among physicians as to the dangers from the entrance into the circulation of small quantities of air. Laborde and Muron²⁶ injected into the external jugular vein of a dog 1,120 cubic centimetres of air in the space of one hour and a half without causing death, and Jürgensen²⁷ into the left femoral artery of a narcotized dog weighing 43½ kilogrammes, 3,650 cubic centimetres in the space of two hours and twenty-five minutes with only

slight disturbance of the respiration and of the action of the heart. Hare,²⁸ likewise, on the basis of experiments, controverts current beliefs in the dangers from entrance of air into veins.

I have come across in the older literature from the days when venesection was a common practice reports of cases in which blood containing bubbles of gas escaped during venesection from veins of the arm.²⁹ In none of these was there evidence that air had gained entrance to the circulation. Maisonneuve³⁰ in incising two gaseous phlegmons of the thigh following compound fracture observed the escape of blood containing gas bubbles from the cut veins, and was able to trace the gas within the veins for a long distance.

It seems to me very improbable that an anaerobic bacillus such as the gas bacillus can multiply in the circulating blood, still this bacillus is less sensitive to the presence of oxygen than many anaerobes, and we do not know whether the loose combination in which oxygen is present in the blood would necessarily prevent its growth under all circumstances.

I see no reason why this bacillus might not multiply in the liver, spleen and most other internal organs, as we know it can do in parts open to inspection during life. We have positive evidence in the cases reported by Graham, Steward and Baldwin and by Dunham that gas bacilli may be conveyed by the circulation from an infected portal of entry—in the one case the puerperal uterus and in the other a urethral wound—to distant parts of the body and there produce subcutaneous emphysema and necrosis. There is no part of the body which offers such favorable conditions for the post-mortem growth of the bacillus as the liver, probably on account of its content of carbohydrate, and if the liver, like the integuments, were open to inspection during life, I believe that we should find evidence that in certain cases the emphysema of this organ, which is such a conspicuous post-mortem phenomenon in instances of invasion by the gas bacillus, had begun during the life of the patient. Emphysema, due to gas bacilli, of mucous membranes open to inspection we know can exist during life. This subject will be considered subsequently.

In the great majority of instances, however, in which gas bubbles are found in the blood and internal organs at autopsy the evidence is in support of the view that the development of the gas is a purely post-mortem phenomenon. Certainly the greatest caution should be exercised in the interpretation of any such cases as vital processes, even in early autopsies without ordinary putrefaction.

One thing which our investigations have established is that the finding of gas bubbles in the blood-vessels and heart within as short a time as one hour after death furnishes in itself no proof of the entrance of air into the circulation. I shall refer later to the question of gaseous embolism in cases of emphysematous gangrene and of physometra.

EMPHYSEMATOUS GANGRENE.

In a few instances we have found in wounds, usually compound fractures or gunshot injuries, in which dirt had gotten in, *Bacillus aerogenes capsulatus*

²⁶ *Therapeutische Gazette*, 1889, 3 s., v, p. 606.

²⁸ Marshall's case reported by May, *Trans. Path. Soc., London*, 1858, ix, p. 157; Durand-Fardel's case also cited by May, and Pirgoff's case in his *Grundzüge d. allg. Kriegschirurgie*, p. 1063, Leipzig, 1864.

²⁹ Cited from Hirschmann and Lindenthal: *Sitzungsab. d. k. Akad. d. Wiss., Math.-Naturw. Cl., Wien*, 1899.

²⁶ *Compt. rend. de la Soc. de Biol.*, 1873, v.

²⁷ *Deutsch. Arch. f. klin. Med.*, 1882, xxxi, p. 458.

without the presence of gas or other evidence that the bacillus was producing any characteristic effects.⁸¹ Such cases have always been watched by the surgeons with anxiety and it is probable that at least in some the early recognition of the bacillus, followed by free incisions and thorough cleansing and disinfection, has warded off a subsequent grave infection. In view of the wide distribution of the gas bacillus in the outer world and in the intestinal contents it is probable that it must not so very infrequently gain access to wounds without securing a foothold. While this innocent behavior, with which we are also familiar in the case of the tetanus bacillus, may sometimes be due to attenuated virulence of the bacillus, it is probably oftener attributable to accessory circumstances, such as the resistance of the patient, the condition of the wound and surrounding tissues, and association with other micro-organisms and with foreign substances.

It is as a cause of that most dreaded of wound complications, emphysematous gangrene, that *Bacillus aërogenes capsulatus* especially claims the interest of surgeons. The classical clinical descriptions of this disease we owe to Maisonneuve,⁸² and to Pirogoff,⁸³ the former giving to it the name "gangrène foudroyante," and the latter designating it "primary mephitic gangrene" or "acute gangrenous edema." Among other more or less common designations are "emphysematous or gaseous gangrene," "gaseous phlegmon," "septic emphysema," "érysipléle bronzé" (Velpeau), "progressive gangrenous edema," "gangrenous septicaemia," and "emphysematous cellulitis."

This wound complication was more common in pre-antiseptic times, especially in military surgery, than it is to-day, but at least 70 cases have been reported during the last quarter of a century. In pre-bacterial days the affection was attributed by some writers to the penetration of air into the tissues, but by most to the decomposition of the tissues, particularly of adipose tissue and bone-marrow, brought by an injury into contact with the atmosphere.

Bottini⁸⁴ in 1871 was the first to demonstrate the infective nature and transmissibility of emphysematous gangrene. Later Gussenbauer also recognized the disease as a definite infection and attributed it to the bacteria of putrefaction. After Pasteur's discovery in 1877 of his "vibron septique," more commonly, since Koch and Gaffky's investigations, designated *Bacillus edematis maligni*, and especially after Chauveau and Arloing's⁸⁵ paper in 1884, cases of emphysematous gangrene have been usually reported, especially in France, as instances of Pasteur's gangrenous septicaemia or Koch's malignant edema. W. Koch's⁸⁶ attempt to identify the disease with symptomatic anthrax (Rauschbrand) was based on faulty bacteriological studies and has met with no confirmation. In 1884 F. J. Rosenbach⁸⁷ reported finding in cover-slip specimens from two cases of traumatic emphysematous gangrene coarse bacilli, some of which had terminal spores. These emphysema bacilli, as he calls them, he was unable to cultivate, only aerobic

methods being employed. It is probable that Rosenbach saw *Bacillus aërogenes capsulatus* in these cases, but without distinguishing it from associated spore-bearing bacilli.

A critical examination of the records of alleged malignant edema in human beings shows that in very few was the organism concerned satisfactorily identified as the genuine malignant edema bacillus. Very often it has been simply assumed without more than a microscopical examination that bacilli found in spreading edematous conditions with or without gas have been those of malignant edema, and even where cultures and animal experiments have been employed the descriptions are frequently so meagre as to leave the identity of the organism wholly in doubt. In France it is usually assumed without any discussion and even without any bacteriological examination that gangrène foudroyante is malignant edema (Pasteur's septicaemia),⁸⁸ and the same ignorance of the present status of this subject is still sometimes encountered in England, Germany and elsewhere. Nevertheless, the investigations of the last seven years, beginning with those of E. Fraenkel, and soon followed by observations of myself and collaborators, have demonstrated that by far the most common and important specific cause of gaseous phlegmons or emphysematous gangrene is *Bacillus aërogenes capsulatus*.

Whether the bacillus of malignant edema can produce an identical or similar anatomical and clinical affection in human beings I regard as an unsettled question. It is certainly remarkable in view of current doctrines in text-books that neither E. Fraenkel nor I, with our relatively large experience, nor indeed, so far as I am aware, any one who has made himself thoroughly acquainted with *Bacillus aërogenes capsulatus*, has encountered an instance of emphysematous gangrene in man caused by the bacillus of malignant edema. The whole subject of human malignant edema is one which needs thorough revision and investigation by more exact bacteriological methods than have yet been applied to it.⁸⁹ I have already mentioned the chief points of difference between the bacillus of malignant edema and *Bacillus aërogenes capsulatus*.

There is a relatively small group of cases of gaseous phlegmon attributed by those reporting them⁴⁶ either to the colon bacillus or the proteus bacillus. In most of these cases anaërobic culture methods were not employed. No one has succeeded in producing experimentally gaseous phlegmon with either of these bacilli, and I think there is good reason to be sceptical concerning their capacity to produce this disease, unless, perhaps, *Bacillus coli* may do so in diabetics.

It is possible that some of those reporting the colon bacillus as the cause of emphysematous gangrene may have confounded with it a facultative anaërobic bacillus which we have isolated from two cases of this disease and which has been studied in my laboratory by Dr. Lanier. It resembles in anaërobic cultures very

⁸¹ Such cases have been reported by Bloodgood, of the Johns Hopkins Hospital, in *Progressive Medicine*, December, 1899, iv, p. 158.

⁸² *Gaz. méd. de Paris*, 1853, p. 592.

⁸³ *Grundzüge d. allg. Kriegschirurgie*, pp. 867 and 1006, Leipzig, 1884.

⁸⁴ *Glor. d. r. Accad. di mod. di Torino*, 1871, 3 s., x, pp. 1121 and 1138.

⁸⁵ *Bull. de l'Acad. de Méd.*, 1884, 2 s., xlii, p. 604.

⁸⁶ *Deutsch. Chir., Lief.*, 9, Stuttgart, 1886.

⁸⁷ *Die Mikro-Organismen bei den Wund-Infektionskrankheiten des Menschen*, p. 91, Wiesbaden, 1884.

⁸⁸ *Bull. de l'Acad. de Méd.*, 1884, 2 s., xlii, p. 604.

⁸⁹ *Deutsch. Chir., Lief.*, 9, Stuttgart, 1886.

⁴⁰ Chlari, v. Dungern, Bunge, Klemm, Hlava, Evans, Grasberger, Hauser, Margarecci, Muscatello, Hirschmann and Lindenthal.

closely *Bacillus aerogenes capsulatus*, but it is capable of aerobic growth also, and then the rods are thinner and more like colon bacilli. It has the power of producing gas abundantly in the blood and tissues of rabbits killed a few minutes after intravenous injection, a power not possessed by genuine colon bacilli. I have already spoken of the importance of this test, which has been employed by none of the writers who have claimed to find colon bacilli as the cause of gaseous phlegmons. This bacillus, when virulent, is capable of causing the same spreading and fatal emphysematous necrosis in guinea pigs and pigeons as is *Bacillus aerogenes capsulatus*.

I have been accustomed to speak of this bacillus, to which I have called attention in previous publications, as the aerobic variety of our gas bacillus. I believe, however, that it is identical with Sanfelice's *Bacillus pseudo-œdematis maligni*,⁴¹ with which he is inclined to identify Klein's "new bacillus of malignant edema."⁴² Chavigny⁴³ has isolated apparently the same bacillus, which he likewise identifies with Sanfelice's *Bacillus pseudo-œdematis maligni* (not to be confounded with the pseudo-œdema bacillus of Liborius), from a case of gaseous gangrene, and he also calls attention to the probability that others may have mistaken it for the colon bacillus. While, therefore, unwilling upon existing evidence to accept the colon bacillus as a demonstrated cause of gaseous gangrene (except perhaps in diabetics), I am of the opinion that an aerobic bacillus, probably identical with Sanfelice's *Bacillus pseudo-œdematis maligni*, is capable of producing this affection, but it is much less frequently concerned than *Bacillus aerogenes capsulatus*.

I have collected 46 cases of emphysematous gangrene, in all of which *Bacillus aerogenes capsulatus* was demonstrated, and, therefore, all reported or observed during the last seven years.⁴⁴ This is a far larger number of cases than has ever been brought together before.

Thirty-two are reported by American observers and only 14 by foreign investigators. Of the former group of cases 16 were observed in Baltimore, most of the cultures having been studied in my laboratory; of the foreign group of cases all are reported from Germany, Austria, Italy and France,⁴⁵ 4 by E. Fraenkel, 1 (not absolutely certain) by Passow, 5 by Hitsch-

mann and Lindenthal, 3 by Muscatello assisted by Gangitano, and 1 by Guillemot.

Cases of gaseous phlegmon in which *Bacillus aerogenes capsulatus* was not demonstrated are not included, although many of these presented the same clinical characters and doubtless in some at least the gas bacillus was the active agent. This is true especially of the cases of gangrène foudroyante, usually without satisfactory bacteriological examination, attributed by French writers to Pasteur's vibrión septique. Gertler's⁴⁶ 8 cases of gaseous phlegmon cannot be utilized for our purposes at all, as they are without any satisfactory bacteriological reports.

A complete analysis of these 46 cases would afford material more than sufficient to occupy this entire address, so that I shall be able to present here only some of the more important points.

Thirty-five of the patients were males, 10 females, and of 1 the sex is not stated. The preponderance of males is explained by the fact that most of the cases were due to severe injuries. Robust workmen in the prime of life furnished the largest contingent of cases.

In 80% of the cases one of the extremities was the seat of the emphysematous gangrene, the lower being affected a little over twice as often as the upper extremities. In several instances the emphysema extended from the thigh to the abdominal wall or from the arm to the subcutaneous tissues of the shoulder and chest. There were three examples of primary emphysematous phlegmon of the abdominal wall; of these 1 following removal of the appendix (Bloodgood), 1 from an unrecognized strangulated Littre hernia (Martin) and 1 affecting the deep tissues of a nephrectomy wound (Muscatello). In all of these the infection is believed to have started from the intestine. In one of Dunham's cases there was emphysematous gangrene (originating in a prostatic abscess opening in the buttock) of the scrotum, penis and anterior abdominal and thoracic subcutaneous tissues. In three instances (Carroll, 2; Dobbin, 1, reported by Bloodgood) the breast and submammary tissues were the primary seat of the disease, all of these resulting from the infusion of salt solution. In one case (Dunham) the gaseous phlegmon appeared at the angle of the lower jaw after incision of a foul submaxillary abscess. In one instance (Welch and Flexner) it started within the pelvis from traumatic rupture of rectum and extended through the sciatic notch down the thigh.

Of especial interest are three examples of multiple or metastatic emphysematous gangrene, one of the forearm and opposite shoulder, another of the thigh and both shoulders, and still another of one shoulder and the buttocks. In the older literature are similar cases; thus Nélaton observed emphysema not only in the injured leg but also in the opposite uninjured extremity. In 1897, Leech⁴⁷ reported without adequate bacteriological examination, a case of emphysematous gangrene of the right leg following about three weeks after injury of the right thumb, which became inflamed, there being no evident local cause of the affection of the leg. These cases are to be explained by transportation of the bacilli through the lymphatic or blood current from the primary focus of entrance.

In all but 5 of the 46 cases the emphysematous gangrene followed traumatism or a surgical operation.

⁴¹ Ann. d. Istit. d'Igiene sper. d'R Univ. di Roma, 1891, n. s., i, p. 395, and Zeit. f. Hyg., 1893, xiv, p. 352.

⁴² Centralbl. f. Bakt., 1891, x, p. 186.

⁴³ Ann. de l'Inst. Pasteur, 1897, xi, p. 860.

⁴⁴ This list includes 16 cases observed in Baltimore, mostly at the Johns Hopkins Hospital, of which 2 are unpublished, and the remaining 14 have been published by Mann (1), Annals of Surgery, 1894, xix, p. 187; Welch and Flexner (6), Journal of Experimental Medicine, 1896, i, p. 5; Martin (1), University Bulletin, 1896, i, No. 3; and Bloodgood (6), Progressive Medicine, December, 1899, iv, p. 154. The notes of an additional unpublished case observed in Manila have been given me by Dr. Flexner. There are also 3 unpublished cases for the records of which I am indebted to Dr. Carroll, of Washington. The references to the remaining 26 cases are as follows: E. Fraenkel (4), Ueber Gasphlegmonen, Hamburg u. Leipzig, 1903; Passow (1), Charité-Annalen, 1895, xx, p. 275; Dunham (6), Bulletin of Johns Hopkins Hospital, 1897, viii, p. 68; Ferguson (1), Transactions of Indiana Medical Society, 1897, p. 339; Erdmann (1), Medical Record, February 5, 1898, p. 205; Le Bouillier (1), Medical Record, March 5, 1898, p. 353; Love and Cary (1), Medical Record, April 8, 1899; Norris (1), American Journal Medical Sciences, 1899, cxvii, p. 195; Hitschmann and Lindenthal (5), Sitzungsber. d. k. Akad. d. Wiss., Math. Naturw. Cl., Wien, 1899, cxviii, Heft. 3, Abth. III, p. 67; Thorndike (2), Boston Medical and Surgical Journal, June 7, 1900, p. 592; Muscatello with Gangitano (3), Riforma med., 1900, II, pp. 508, 519 and 530; Guillemot (1), Compt. rend. Soc. de Biol., 1898, 10, s., v, p. 1017. A few other cases in which the gas bacillus was found are not reported with sufficient detail to be available for analysis. It is safe to say that *Bacillus aerogenes capsulatus* has now been found in at least 50 cases of gaseous gangrene.

⁴⁵ Soupault and Guillemot's (Compt. rend. Soc. de Biol., 1898, 10, s., v, p. 1017) three cases of gaseous abscess came to my notice too late to be included, and perhaps should not be classed under emphysematous gangrene. All were relatively benign.

⁴⁶ Ueber Gasphlegmonen. Inaug.-Diss. Halle, 1898.

⁴⁷ Quarterly Medical Journal (Sheffield), 1896-97, v, p. 237.

The injuries were as follows: Compound fracture, 18; bullet and gunshot wounds, 7; infusion of salt solution, 3; hypodermic injections, 2; ligation of the femoral artery for aneurism, 3; external urethrotomy, 2; traumatic rupture of the rectum, removal of the appendix, prostatic abscess following self-catheterization, operation for strangulated Littré hernia, incision of a foul submaxillary abscess, and nephrectomy, each 1. Of the 5 non-traumatic cases the gaseous gangrene followed erysipelas in 1, was consecutive to apparently spontaneous gangrene in 2, whether diabetic or not is not stated, and was without apparent explanation in 2 (Fraenkel, Case 2, and Passow).

Compound fractures, and next bullet and gunshot wounds, occupy by far the most prominent place in this list, each of the other various causes being represented only by scattered cases. Those injuries in which there are much laceration and crushing of tissue, comminution of bone and grinding of dirt, bits of clothing or other foreign bodies into the wound are the ones most likely to be followed by emphysematous gangrene. That, however, severe traumatism is not an essential factor is shown by the 5 cases (10% of the entire number) following hypodermic injections and infusion of normal salt solution. These latter, however, were all of patients whose vital forces were greatly depressed, namely, by Asiatic cholera, typhoid fever, surgical shock, or post-partum hemorrhage. There is good reason to believe that the intact tissues of human beings in health possess marked resistance to the gas bacillus.

In the great majority of cases it was evident that the gas bacillus was introduced through the wounded skin from without. In three instances (removal of appendix, strangulated hernia, and traumatic rupture of the rectum) the infection undoubtedly came from the intestine. This was also the probable source of infection in one of Muscatello's cases (gaseous phlegmon in the site of an extirpated kidney). With our present knowledge of the frequent, if not regular, presence of *Bacillus aerogenes capsulatus* in the intestine, there is nothing surprising in this mode of infection. In three of Dunham's cases the infection followed injury of the urethra, and here also the bacilli may have come from the intestine. In one of his cases (gaseous phlegmon at angle of the jaw) it was suggested that the bacilli gained entrance through decayed teeth.

Bloodgood thinks it probable that in one of his cases the gas bacilli were brought by the circulation to the seat of infection. In this case the femoral artery was ligated for traumatic arteriovenous aneurism in the popliteal space. There was no primary infection of the wound, but gangrene of the foot and leg ensued and on incision gas bubbles were found in the blood of the aneurismal sac and the tissues. With what we know about the entrance of intestinal bacteria into the circulation, there is nothing improbable in Bloodgood's opinion. The clot in an aneurism and tissues robbed of their nutrient supply would offer little or no resistance to the growth of bacilli which might reach them or their immediate neighborhood through the circulation, and the conditions would be anaerobic. It was indeed a case of aneurism in which I first found the gas bacillus, and here the clot was swarming with bacilli. It is interesting to note that three of the cases of emphysematous gangrene in

my list followed ligation of the femoral or popliteal artery for aneurism.

Pirogoff⁴⁸ distinguished clinically two groups of cases of traumatic emphysematous gangrene. He described under the name "primary mephitic gangrene" cases in which the emphysema appears within two days after the injury, the "local stupor" passing without inflammatory reaction into crepitating gangrene. Here the emphysematous necrosis spreads rapidly, the patient sinks into collapse with an icteroid hue of the skin, small, thready pulse and cold sweats, and death occurs usually within a few days after the onset. This type of the disease corresponds to Maisonneuve's *gangrène foudroyante*. In the second group, designated by Pirogoff also as "acute gangrenous edema," there is reaction from the primary "local stupor" of the tissues, the emphysema is preceded and accompanied by local edematous or purulent inflammation, is associated with febrile reaction, often appears later after the injury and spreads less rapidly, and presents in general a more varied anatomical and clinical picture than the first class of cases.

Hitschmann and Lindenthal consider that Pirogoff's first group corresponds especially to cases of pure infection with the gas bacillus, and his second group to mixed infections. Erdmann is also of the opinion that in the unmixed infections the emphysematous necrosis spreads more rapidly and is more likely to terminate fatally. On the other hand Muscatello and Gangitano, who also divide the cases into two groups — pure infections and mixed infections — hold that the mixed infections are characterized by the rapidly progressive form of emphysematous gangrene, while the pure infections, at least in their early stage, show little tendency to spread beyond the injured tissues. According to the last named authors the gas bacillus is incapable of exerting any pathogenic action upon healthy tissues, but attacks only tissues already altered in their vitality by injury, other pathogenic micro-organisms, toxins, or other depressing factors.

The study of our cases has not enabled me to adopt either of the two conflicting opinions just stated. Of the collected 46 cases, 30 were mixed infections, 14 were pure, and in 2 there is no clear statement on this point. The most common associated bacteria were the pyogenic streptococci and staphylococci. Other forms found occasionally were *Bacillus coli*, proteus, pyocyanus, tetanus, Sanfelice's *Bacillus pseudo-œdematis maligni*, and uncultivable, often spore-bearing, bacilli. It seems probable that the bacillus of malignant edema, being a common inhabitant of the soil, must occasionally, like the tetanus bacillus, be present, but it was not isolated from any of these cases. My experience is that if reliance be not placed exclusively upon cultures, but careful microscopical examinations be also made, instances of unmixed infection with the gas bacillus are rare. It is by no means always easy to determine whether associated bacteria are exerting pathogenic action or not. Pyogenic cocci may be present without producing pus or marked inflammatory reaction.

We have found rapidly progressive forms of emphysematous gangrene both with pure infections with the gas bacillus and with mixed infections, and on the other hand we have observed with both types of infection cases in which the tendency to spread is much

⁴⁸ *Grundzüge d. allg. Kriegschirurgie*, p. 1008, Leipzig, 1864.

less marked. In all of the cases with much purulent inflammation mixed infection was present, but aside from this feature the division of the cases into pure and mixed infections does not, according to our experience, correspond to different, sharply marked, clinical features. Pirogoff's classification is doubtless of clinical value, but there is every gradation between the two groups.

I cannot agree with Muscatello and Gangitano, whose investigations of emphysematous gangrene are of great value, that the gas bacillus is incapable of attacking healthy tissues. Virulent cultures, even in small doses, can produce rapidly spreading gaseous phlegmons when inoculated into the subcutaneous tissues of susceptible animals, such as guinea pigs and pigeons. In human beings the emphysema may extend very rapidly into the healthy tissues, frequently outstripping in its advance the inflammatory edema. This may occur in pure, as well as in mixed, infections with the gas bacillus. It is true, as urged by Muscatello and Gangitano, that toxins derived from the bacilli may prepare the tissues for the invasion and action of the advancing bacilli, but the same explanation has been put forward for the spread of other pathogenic bacteria in healthy tissues. In asserting that the gas bacillus may attack healthy tissues, I would not be understood as minimizing the great importance of the various accessory causes of emphysematous gangrene which act by lowering the vitality of the tissues or the general resistance of the patient or as failing to recognize the marked resistance to infection by the gas bacillus offered by the healthy tissues, a resistance to which I have previously called attention and which I shall have occasion further to emphasize.

Gas may appear in the tissues as early as eight hours after the injury. In a case of gaseous phlegmon following a bullet wound of the knee joint, reported by Welch and Flexner, Dr. Bloodgood recognized gas in the joint⁴⁰ and surrounding tissues just twenty hours after the injury. In a case of Dr. Tiffany's which we have reported, death from emphysematous gangrene, due to pure infection with the gas bacillus, occurred forty-eight hours after a fall causing a compound comminuted fracture of the patella with grinding of the underclothing into the wound. There was no other injury of the body. Any one who has seen one of these rapidly fatal cases of spreading traumatic, emphysematous gangrene will receive an impression which he will never forget.

The anatomical and clinical study of uncomplicated emphysematous gangrene demonstrates that the disease is not, as many formerly supposed, simply an intense variety of ordinary phlegmonous inflammation or cellulitis, but is a disease *sui generis*. It may be combined with phlegmonous inflammation, but then some other micro-organism, usually the streptococcus, is associated with the gas bacillus.

In typical uncomplicated cases the lesions consist in necrosis of all the tissues, the presence of gas in the interstices, infiltration with blood, evidences of the mechanical action of the gas, and exudation of a variable amount of bloody serum. The amount of gas varies much in different cases. There may be only a few bubbles or the tissues may be everywhere blown up with gas. The nuclei disappear by karyolysis. The

notable thing in most cases is a nearly complete absence of leucocytes and of cellular reaction, although in a few instances, even of pure infection, I have found leucocytes in considerable number, and even purulent foci, but generally at a distance from the primary necrosis. As will be shown later, *Bacillus aerogenes capsulatus* in certain situations is capable of setting up purulent inflammation. In one of our cases, reported by Bloodgood, Dr. Cushing found gas bacilli without gas in a small subcutaneous abscess of a stump two months after amputation of the thigh for emphysematous gangrene of the leg, the amputation having been followed by uninterrupted convalescence.

After death there may be a rapid extension of the subcutaneous emphysema, and at autopsies made a few hours after death gas bubbles may be found in the heart, vessels, liver and other organs, but as to this occurrence there is no rule. As I have already explained, wide-spread distribution of gas in the blood and organs in early autopsies indicates entrance of the bacilli into the circulation during life.

As is to be expected from the etiology of many of the cases of emphysematous gangrene, emboli of fat and of bone-marrow cells are common in the pulmonary capillaries, but I do not know that in any case they contributed to the fatal result.

The prognosis of emphysematous gangrene is more favorable to-day than before the antiseptic period. The disease terminated fatally in 59½% of the cases in my list. In the cases observed and treated at the Johns Hopkins Hospital—10 in number—the fatality was 50%, but of these one was a gaseous phlegmon of the pelvis extending to the thigh, resulting from traumatic rupture of the rectum; a second was a gaseous phlegmon of the abdominal wall following removal of the appendix and complicated with diffuse gangrenous peritonitis, and a third case terminated twenty-five days after disappearance of a gaseous phlegmon of the thigh (treated by incisions) from a late streptococcus infection, gas and the gas bacillus having disappeared. Of the two remaining fatal cases, in one—emphysematous gangrene following compound fracture of the thigh—amputation was refused by the patient until the fourth day, when he was in a state of collapse and died fifteen hours later, and in the other—compound fracture of the skull and both lower extremities—the patient died thirty hours after the accident, having never regained consciousness. When the disease is accessible to surgical treatment, is not complicated by other grave conditions, and is promptly recognized and treated, the prognosis, according to the experience of my surgical colleagues, Professor Halsted and Dr. Bloodgood, is not very unfavorable.

The clinical evidence seems to me to favor the view that, at least in most uncomplicated fatal cases, death is due to toxemia. Norris was unable to demonstrate the presence of strong toxins in artificial cultures of *Bacillus aerogenes capsulatus*, but, as is well known, the same difficulty is encountered with many other pathogenic bacteria which are believed to produce poisons in the human body. Muscatello is also of the opinion that the constitutional symptoms are attributable to toxemia.

The suggestion that death may be due to gaseous embolism is not new. Pirogoff and other of the older observers knew that gas bubbles may be found within the heart and vessels very soon after the death

⁴⁰ It is to be regretted that in the cases reported by Prutz (Deutsch. Zeit. f. Chir., 1898, xlviii, p. 591) as traumatic entrance of air into the knee joint, no bacteriological examination was made.

of patients from emphysematous gangrene. In the discussion on Langenbeck's paper on traumatic infiltration before the Society of German Military Surgeons in 1870, Senator⁶⁰ advocated the idea that death is caused by gas embolism. While the possibility of this occurrence as the cause of death may be admitted, there is at present no proof of this opinion. Gas bubbles are by no means always found in the blood and organs after death from emphysematous gangrene, and the clinical histories of those in which they are found post mortem do not appear to differ from those when they are absent. In experimental gaseous phlegmons in guinea pigs there is no evidence of the presence of gas bubbles in the circulation during life.

In 1 of our cases (Mann) death resulted from tetanus, and Vernieuil⁶¹ has reported 3 cases, which without bacteriological examination he calls malignant edema, where also tetanus intervened. There is nothing surprising in this association when one considers that the home of the tetanus bacillus, like that of the gas bacillus, is the soil. The period of incubation for tetanus is longer than for infection with the gas bacillus, the former appearing rarely before the seventh day, and the latter usually within two or three days after the injury.

Prophylactic measures against emphysematous gangrene are sufficiently obvious from the etiological factors which have already been considered. It is important in wounds of the character most frequently followed by this complication to search microscopically and by cultures for the gas bacillus. The examination of cover-slips will usually suffice for a probable diagnosis. I have already cited instances in which this bacillus has been detected before the onset of emphysema and in which there is good reason to think prompt surgical treatment warded off severe infection. The possibility of infection from the intestinal canal, as well as from external sources, is to be borne in mind.

The cases were treated either by free incisions or by amputation or both. The results were better after amputation than after simple incisions. Of the cases of emphysematous gangrene affecting primarily the extremities, the recoveries numbered 68% after amputation, and 33½% after incision without amputation. Careful study of individual cases shows that amputation is by no means always necessary. Everything depends upon early recognition of the nature of the infection. Dr. Bloodgood⁶² from a relatively large experience says: "If the infection is recognized early, and the destruction of the soft parts and bone is not extensive, free incisions with immediate continuous bath treatment should be tried. If the general symptoms of infection are not immediately relieved, amputation should be done. If, however, the infection is recognized late, one should take no risk but amputate at once. . . . An early diagnosis will probably save life, and from many observations an amputation may not always be necessary."

A similar position as to prognosis and treatment is taken by Muscatello and Gangitano in their valuable paper on gaseous gangrene, in which they also emphasize the value of abundant irrigations with disinfectant and oxidizing solutions. In the service of

Dr. Halsted at the Johns Hopkins Hospital the continuous bath treatment has been found useful. Hitschmann and Lindenthal are certainly mistaken in their assertion that incisions are usually without favorable effect and that early amputations offer the only chance of recovery. As pointed out by Thorndike and others, recovery may follow amputation, even when it is impossible to remove the whole of the diseased tissues.

UTERINE INFECTIONS.

Knowledge of *Bacillus aerogenes capsulatus* is of not less interest and importance to the obstetrician than to the surgeon. Infection of the puerperal uterus by this micro-organism leads to a variety of morbid conditions, some comparatively mild, others of the utmost gravity.

The wide distribution of the gas bacillus in the intestinal canal and the outer world renders as explicable the occasional presence of this bacillus in the female genital tract as that of the colon bacillus in the same situation. Lindenthal⁶³ found the gas bacillus in the vagina without the presence of gas or other pathogenic effects, twice out of 6 puerperal cases examined. According to the observations of others, Lindenthal's experience would seem to be exceptional. As with so many other pathogenic bacteria, the mere presence of the organism upon exposed surfaces does not necessarily signify infection.

I shall consider the uterine infections by the gas bacillus under the headings of emphysema of the fetus, puerperal endometritis, physometra, emphysema of the uterine wall, and puerperal gas-sepsis, although these conditions may be associated with each other.

Emphysema of the fetus.—The occurrence of emphysema in the dead fetus in utero has been known for centuries,⁶⁴ but it was not until 1897, when Dobbin published his paper on "Puerperal Sepsis due to Infection with the *Bacillus Aerogenes Capsulatus*,"⁶⁵ that the cause of this condition was determined to be invasion by the gas bacillus. In this case gas and the gas bacillus were both recognized during the life of the patient in the fetus, the placenta and the cavity of the uterus, and after death there was general gas formation throughout the body.

Dr. Dobbin has kindly given me the notes of a second unpublished case observed by him. He was called to see a woman in difficult labor, upon whom repeated attempts at delivery of a dead fetus had been made. Upon examination he recognized crepitation of the caput succedaneum while the fetus was still in utero. Upon delivery the fetus was emphysematous with foamy organs. The gas bacillus was found in pure culture in the fetus and mixed with other bacteria in the amniotic fluid. No gas was recognized in the uterus after delivery. The patient made a good recovery without evidence of sepsis.

Meige and Krönig⁶⁶ have observed three instances of fetal invasion by the gas bacillus and have brought strong evidence that usually the invasion is through the mouth of the fetus, the bacilli being taken into the lungs or stomach by inspiring or swallowing am-

⁶⁰ Wien. klin. Woch., 1897, pp. 3 and 35.

⁶⁴ It is usually stated that this condition was known to Celsus, but he does not expressly mention the presence of gas, although this is to be inferred. In the chapter on extraction of the dead fetus, he says: "Solot otiam evenire, ut is infans humore distendatur, ex quo eo profudit foedi odoris sanies." Milligan's "Celsus," p. 394, Edinburgh, 1831.

⁶⁵ Bulletin of the Johns Hopkins Hospital, 1897, viii, p. 24.

⁶⁶ Bakt. des weibl. Genitalkanals, Teil II, p. 167, Leipzig, 1897.

⁶¹ Deutsch. militärärztl. Zeit. 1872, I, p. 260.

⁶² Semaine Méd., 1890, p. 403.

⁶³ Deutsch. Zeit. f. Chir. 1898, xlviii, p. 174.

niotic fluid. In their cases the bacilli were not found in the part of the umbilical cord attached to the placenta, but in Dobbin's first case this, as well as the placenta itself, was infected with the gas bacillus. The amniotic fluid within the intact membranes, as is well known, is usually sterile, and only exceptionally becomes infected before rupture of the membranes, so that the infection of the fetus from this source is generally after this rupture. As shown by Menge and Krönig, all grades of invasion of the fetus by the gas bacillus occur, so that there may be only a small amount of gas, and this limited to the lungs or the alimentary canal or both. The medico-legal importance of not mistaking for air this gas in the fetal lungs produced by gas bacilli should be emphasized.

As is well known, fetal emphysema is usually unattended with danger to the mother. In 2 of the 5 cases due to *Bacillus aerogenes capsulatus* in my list the puerperium was even without rise of temperature, in 2 there was mild fever, but in Dobbin's first case there was rapidly fatal gas sepsis.

Puerperal endometritis.—Under the heading "gas-sepsis" will be considered cases of acute uterine infection with the gas bacillus followed by invasion of the blood and organs by this organism. Here it may be mentioned that *Bacillus aerogenes capsulatus* may be present in the uterus, usually in association with other bacteria, in both mild and severe cases of puerperal endometritis without the recognition of gas in the fetus or the uterine cavity or wall. An example of such a case is an unpublished one in the service of Dr. J. Whitridge Williams, of which the notes have been furnished me by Dr. Dobbin. A woman with rachitic pelvis, upon whom delivery by forceps had been attempted before admission to the Johns Hopkins Hospital, was there delivered by craniotomy. There was no gas in the fetus. Forty-eight hours later *Bacillus aerogenes capsulatus*, together with streptococci, was found in the uterine lochia. No gas was detected. The patient developed fever, but recovered.

In 2 cases, one reported by Dobbin⁵⁷ and the other by Blumer,⁵⁸ the gas bacillus, although not identified with absolute certainty, was probably present in the puerperal uterus in association with the typhoid bacillus.

Physometra.—Distension of the uterine cavity with gas (physometra, or tympany of the uterus) was present in Dobbin's first case, already cited, and is often associated with emphysema of the dead fetus, but may occur without the latter and even in the non-pregnant uterus. This curious condition was formerly ascribed to entrance of air or to ordinary putrefaction,⁵⁹ but it is now known to be the result of the activity of gas-producing bacilli.

Since the observations of Lindenthal,⁶⁰ reported in 1898, it cannot be doubted that *Bacillus aerogenes capsulatus* is the chief cause of physometra. He found this bacillus in five cases during life and reproduced the condition experimentally in guinea pigs. He is justly sceptical of the correctness of the previous reports of Gebhard⁶¹ concerning the agency of the colon bacillus in generating gas within the uterus. We

know from Theobald Smith's investigations that the colon bacillus can produce gas only from carbohydrates, whereas it is the most distinctive biological attribute of our gas bacillus that it can produce gas from proteids. Until it has been shown that the amniotic fluid and uterine contents may under any conditions contain enough carbohydrate to explain the development of gas by the colon bacillus, there is every reason to question the claims for this bacillus as a cause of tympany of the uterus.⁶²

My list of cases contains ten instances of physometra in which *Bacillus aerogenes capsulatus* was demonstrated. Although, as some of our cases show, this condition may be associated with invasion of the bacilli into the wall of the uterus and by acute gas sepsis, these occurrences are exceptional and the prognosis is in general a favorable one. Most of the cases furnish a good illustration of the resistance of living human tissues to the action of the gas bacillus. Doubtless in these cases the bacilli grow simply in the amniotic fluid after rupture of the membranes, and in the dead fetus, these offering no vital resistance, whereas we must suppose that the intact uterine wall offers ordinarily an effective resistance to the invasion and multiplication of the gas bacillus. That occasionally the bacilli may find other dead material in the uterus, as in sloughing myomata and cancers, is evident from the histories of some cases of physometra.

Emphysema of the uterine wall.—Far graver in significance is septic emphysema of the uterine wall, of which Halban⁶³ has recently reported an interesting case due to *Bacillus aerogenes capsulatus*. Graham, Steward and Baldwin and P. Ernst were the first to demonstrate this bacillus in this condition, their papers, to which reference has already been made, appearing simultaneously in August, 1893. Eleven instances of emphysema of the wall of the uterus, all puerperal, have been reported, of which 5 were recognized during life. In all but Halban's case there was also physometra, and this would seem to be a necessary accompaniment unless the cervical canal is open, so as to permit the escape of the gas from the uterine cavity. All of the cases were fatal, and in most gas was found at autopsy in the blood and internal organs.

Subperitoneal emphysema has been observed after rupture of the uterus, Dischler⁶⁴ having collected reports of 14 cases. In most instances this has been attributed to entrance of air, but I think that it is safe to predict that the gas bacillus will be found in similar cases in the future, if proper methods for its detection are employed. I know, however, of no instance of this condition in which it has been looked for.

Puerperal gas sepsis.—I have adopted from Halban the term "gas sepsis" as a convenient one, although perhaps open to criticism, to designate the important group of fatal puerperal cases in which gas bubbles are found at early autopsies in the heart and vessels and often also in the organs and tissues under conditions where we must suppose that gas bacilli and possibly gas have passed from the uterus into the circulation during life.⁶⁵ Here, in my opinion, belong most of the cases which have been reported as deaths

⁵⁷ *American Journal of Obstetrics*, 1898, xxxviii, p. 185.

⁵⁸ *Ibid.*, 1899, xxxix, p. 42.

⁵⁹ The older hypotheses and records on physometra and emphysema of the fetus are fully presented by Staudé: *Zeit. f. Geb. u. Gynäk.*, 1878, iii, p. 191.

⁶⁰ *Monats. f. Geb. u. Gynäk.*, 1898, vii, p. 269.

⁶¹ *Zeit. f. Geb. u. Gynäk.*, 1893, xxvi, p. 480, and 1897, xxxvii, p. 182.

⁶² Halban (*Monats. f. Geb. u. Gynäk.*, 1900, xi, p. 102) states that he has found lactose once in the amniotic fluid of a normal puerperia. Further studies of this subject are needed.

⁶³ *Monats. f. Geb. u. Gynäk.*, 1900, xi, p. 88.

⁶⁴ *Arch. f. Gynäk.*, 1898, lvi, p. 199.

⁶⁵ Gas sepsis in this sense occurs also in other infections with the gas bacillus than the uterine.

due to the entrance of air into the uterine veins. This opinion, which I expressed in my first communications on the gas bacillus in 1891 and 1892, received prompt confirmation in the papers of Graham, Steward and Baldwin and of P. Ernst, in August, 1893, and has since been strengthened by other similar observations. Cases described by Wendeler⁶⁶ as sepsis acutissima belong also in the same category.

My list includes 12 puerperal cases in which gas bubbles and the gas bacillus were found at autopsy in the blood or organs, but in only 6 of these does it seem to me conclusive or extremely probable that the infection occurred during life.⁶⁷

The most remarkable of these cases is that reported by Graham, Steward and Baldwin, of a woman upon whom abortion had been recently produced, who during the four hours immediately preceding death became emphysematous over nearly the whole body. At the autopsy gas and gas bacilli were found everywhere throughout the body. In Dalton and Bremer's⁶⁸ case, also one of criminal abortion, an emphysematous swelling of the arm and pectoral region was likewise recognized during life. These cases are of importance as demonstrating the invasion of the body by the gas bacillus from the uterus while the blood is still circulating. In Halban's and Dobbin's cases gas was recognized also during life within the wall or cavity of the uterus.

In the majority of cases of puerperal gas-sepsis there has been some operative interference preceding infection, such as criminal abortion, forced delivery for placenta previa or other causes, or the manipulations of an unskilled midwife. The fulminating character of the infection, death being sometimes very sudden, is a notable feature of many of the cases.

In a case of attempted criminal abortion reported by Perkins,⁶⁹ the patient, according to the statement of the practitioner in whose office death occurred, died suddenly, and at the autopsy twelve hours later in cold weather, gas was found in the vena cava, heart, and other vessels, with evidences of injury to the pregnant uterus. The case was reported by Perkins as one of death from air embolism, and certainly with as much and even more plausibility than most cases thus reported. After the publication, Dr. Perkins, upon the request of Dr. Dobbin, was so good as to send the uterus, well preserved in alcohol, to my laboratory, where Dr. Dobbin demonstrated in the uterine vessels and tissue bacilli morphologically and in staining reaction identical with *Bacillus aerogenes capsulatus*.⁷⁰

I would not be understood to deny the possibility of the occurrence of fatal air embolism from the uterus. A very few of the reported cases are difficult to interpret upon any other supposition, but I do claim that the foundations of this doctrine have been seriously shaken by our discovery and investigations of the gas bacillus, and that no case, however plausible, can be considered as positively proven without a satisfactory bacteriological examination. Did we not know how long it takes new knowledge, especially

that originating in this country, to penetrate throughout the medical world, it would be amazing that cases should still continue to be reported, as they are,⁷¹ of deaths ascribed to air embolism without any bacteriological examination or even any reference to the possibility of any other explanation. I am not aware that in any instance of alleged air embolism, a bacteriological examination has been made which would exclude the presence of gas-forming bacteria.

Whether, as suggested by Staude, in any of the cases with gas within the uterine cavity death is attributable to gaseous embolism is, I think, an open question. It is possible, although I know no proof of it, that in some of the cases of sudden death following immediately after some manipulation or operation on the pregnant uterus and attributed to air embolism, gas, generated by bacteria, may have existed under pressure within the uterine cavity and have entered wounded veins in sufficient amount and so suddenly as to have caused death.

To what extent the free gas found in the blood-vessels, heart and internal organs, even very soon after death from what has been described as puerperal gas-sepsis, is there during life is a question difficult to answer. I have already considered this subject, and in this connection will again emphasize the importance of caution in interpreting the presence of gas in these situations as a vital phenomenon, although there is evidence that it may be such.

INFECTIONS OF THE URINARY TRACT.

There is evidence that the urinary tract may not only be a portal of entrance for the gas bacillus into the circulation or adjacent tissues but also be itself the seat of infection by this organism. Unfortunately for the decisive interpretation of many of these cases, *Bacillus aerogenes capsulatus* has, so far as I am aware, hitherto been found in the urinary tract only after death, although in some instances so soon thereafter and under such conditions that its presence during life cannot be doubted.

I have already called attention to instances of emphysematous gangrene following external urethrotomy and other operations on the urinary passages.

Among the cases of general invasion of the blood and organs (foamy organs) by the gas bacillus observed by myself and others are several in which the portal of entry was the urethra, bladder or other part of the urinary tract.⁷² In a case of urethral stricture with cystitis, for which perineal section had been done, reported by Welch and Flexner, gas bacilli were found three-quarters of an hour after death in large numbers in the bladder, ureters and renal pelvis and a few gas bubbles and gas bacilli were already present in the blood of the right ventricle. In Howard's case of meningitis caused by the gas bacillus, to be cited subsequently, he considers that the portal of entry was the urinary tract.

Gas, generated by *Bacillus aerogenes capsulatus*, has been found in the urinary passages in 6 cases which have come to my notice.⁷³ The gas may be either free in the cavity of the bladder, ureters or renal pelvis, or contained within submucous blebs, or in both situations.

⁷¹ Zorn (Münch. med. Woch., 1898, p. 567) may be cited as an example. Gas limited to the right heart may occur from invasion of the gas bacillus.

⁷² Such cases are reported by Welch and Flexner, Goebel, Dunham, and Howard in papers already cited.

⁷³ These do not include some instances of very extensive post-mortem emphysema of the organs with gas everywhere throughout the body.

⁶⁶ Monats. f. Geb. u. Gynäk., 1896, iv, p. 581.

⁶⁷ These are the cases reported by Graham, Steward and Baldwin, P. Ernst, Krönig and Menge, Dobbin, F. C. Wood (Medical Record, April 15, 1899), and Halban, to whose papers references have already been given.

⁶⁸ American Journal Medical Sciences, 1888, xcv, p. 594. This infection, although attributed to the bacillus of malignant edema, was probably due to the gas bacillus.

⁶⁹ Boston Medical and Surgical Journal, 1897, cxxxvi, p. 154.

⁷⁰ Dobbin has reported his examination with further notes of this case in the Monats. f. Geb. u. Gynäk., 1897, vi, p. 375.

Welch and Flexner⁷⁴ have reported an instance of pneumaturia in a diabetic man in whom six hours after death, without trace of cadaveric decomposition, the urinary bladder was found filled with frothy urine containing *Bacillus aerogenes capsulatus* in pure culture. This case indicates that the colon bacillus and *Bacillus lactis aerogenes* are not the sole causes of pneumaturia in diabetics. Dr. Flexner has given me the notes of a second case of pneumaturia upon which he made the autopsy at the University Hospital, Philadelphia. This was of a patient with chronic cardiac disease who had been catheterized twenty-eight hours before admission and who died thirty hours after admission. At the autopsy, made one hour and a half after death, about 60 cubic centimetres of frothy urine were found in the bladder, from which *Bacillus aerogenes capsulatus*, together with *Staphylococcus aureus* and *Streptococcus pyogenes* (no colon bacilli), was cultivated. Neither gas nor gas bacilli were found elsewhere in the body. The mucous membrane of the bladder was edematous. There can be little doubt that in this case the gas bacillus was introduced by the catheter into the bladder.

In one of Welch and Flexner's cases (Case XVIII) of hypertrophied prostate with pyoureter and pyonephrosis, the renal pelves and ureters were found at autopsy distended with gas and containing pus mixed with bubbles of gas. Small gas cysts were present in the mucous membrane of the renal pelves. Neither gas nor gas bacilli were present outside of the urinary organs. In this case cocci and colon bacilli were associated with the gas bacillus.

In a case of Dr. Kelly's, of which the full records have been given me by Dr. Miller,⁷⁵ there was pneumaturia demonstrated by cystoscopic examination and ureteral catheterization to come exclusively from the inflamed left renal pelvis and ureter. Among cocci and other bacteria were found on cover-slips bacilli morphologically resembling *Bacillus aerogenes capsulatus*, but unfortunately no anaerobic cultures were made. None of the bacteria which grew aerobically produced gas in lactose agar. This case is interesting as demonstrating that the gas may come exclusively from one renal pelvis and ureter, but the micro-organism producing the gas was not satisfactorily demonstrated. It seems certain that it was an anaerobic organism, and from the microscopical appearances may have been the gas bacillus.

The subject of submucous gas cysts will be considered subsequently, but here it may be mentioned that besides the gas cysts in the renal pelves noted by Welch and Flexner in the case already cited, Goebel found gas blebs containing in pure culture *Bacillus aerogenes capsulatus* beneath the mucous membrane of the urinary bladder, without gas elsewhere in the body, and Dunham has reported a similar condition of the bladder in a case of emphysematous gangrene with general invasion of the blood and organs by the gas bacillus.

Bacteria have been found also in emphysema of the bladder (cystitis emphysematosa) by Eisenlohr,⁷⁶ Camargo⁷⁷ and Kedrowsky,⁷⁸ but it is impossible

from the authors' descriptions to identify their bacteria. Kedrowsky considers the bacillus isolated by him as allied to *Bacillus aerogenes capsulatus*, but less sensitive to oxygen. Perhaps it was Sanfelice's *Bacillus pseudo-œdematis maligni*, to which I have already referred, but Kedrowsky's description of his cultures hardly inspires confidence in their purity.

Welch and Flexner, and Howard have reported finding the gas bacillus in association with other bacteria in inflammatory lesions of the bladder, renal pelvis and kidneys, without the detection of gas. Howard considers that in one of his cases the bacillus was concerned in the etiology of suppurative lesions of the kidneys, but in this case the colon bacillus and *Streptococcus pyogenes* were also present.

INFECTIONS DERIVED FROM THE GASTRO-INTESTINAL CANAL.

Mention has already been made of the frequent, if not constant, presence of *Bacillus aerogenes capsulatus* in the intestinal canal, of gaseous phlegmons originating from this source, and of the readiness with which intestinal bacteria may gain access to the genito-urinary tract.

The intestine is by far the most common source of the gas bacilli found together with gas bubbles in the blood and organs at autopsies. This invasion may occur either with or without definite intestinal lesions, and is probably in the majority of cases an agonal or post-mortem event. The mode of distribution and spread of the bacilli in these cases has been well described by Howard,⁷⁹ whose experience has been exceptionally large with this class of affections. Especially demonstrative of invasion of gas bacilli from the intestine, usually post mortem, is the occurrence of gas bubbles limited to the neighborhood of the intestine, as in the intestinal wall, within the portal or mesenteric veins or lymphatics, in the subperitoneal tissue, mesentery and omentum, around the pancreas, in the mesenteric glands, and especially in the loose tissue near the gall-bladder and in the porta of the liver, without gas in more remote situations. I have seen examples of each of these occurrences in very early autopsies without ordinary cadaveric decomposition.

Local gastro-intestinal lesions.—Interstitial emphysema of the gastro-intestinal wall will be considered subsequently.

Howard has described several cases with larger or smaller areas of superficial necrosis of the mucous membrane of the stomach and intestine, in which gas bacilli were present in large numbers. These areas, which may occur either with or without gas cysts, are found most frequently beneath the folds of the valvulae conniventes and are characterized by absence of nuclear staining and disintegration of the cells and tissue, usually without marked inflammatory reaction.

Bacillus aerogenes capsulatus may undoubtedly be a cause of meteorism. Instances of this are reported by Welch and Flexner, and by Howard.

Pneumoperitonitis with and without perforation.—My records include 13 cases of diffuse peritonitis in the exudate of which *Bacillus aerogenes capsulatus* was found. Eleven of these were in autopsies made either by Dr. Flexner or myself, 7 having already

⁷⁴ Case XIII of our list in *Journal of Experimental Medicine*, 1896.

⁷⁵ This case is briefly reported by Kelly and MacCallum, *Journal American Medical Association*, 1898, *xxi*, p. 376, whose paper may be consulted for the full literature of pneumaturia.

⁷⁶ Ziegler's *Beiträge*, 1888, *iii*, p. 101.

⁷⁷ *Thèse de Genève*, 1891.

⁷⁸ *Centralbl. f. allg. Path. u. path. Anat.*, 1898, *ix*, p. 817.

⁷⁹ Contributions to the Science of Medicine, dedicated by his Pupils to William Henry Welch on the Twenty-fifth Anniversary of his Doctorate, p. 491, Baltimore 1900.

been published by us in 1896. The remaining 2 cases (both being perforations of gastric ulcers) have been reported by Page,⁸⁰ and by Pratt and Fulton.⁸¹ It was the observation of these cases which first called my attention to the frequent presence of the gas bacillus in the intestine.

Ten of the cases were perforative and 3 were non-perforative. Of the former, 4 were the result of perforation of typhoid ulcers, 4 of gastric ulcers,⁸² 1 of strangulated gangrenous intestine and 1 of a cancerous ulcer of the duodenum. In the last case (autopsy fourteen hours after death) the exudate was sero-fibrinous and the gas bacillus was found in pure culture⁸³ and abundantly in the peritoneal cavity and was absent from other organs and the blood. In the other perforative cases the gas bacillus was mixed with other bacteria, although in some instances it predominated. In all of the cases the abdomen was greatly distended with gas and usually there was great tympanites.

I attach especial importance to the case fully reported by Welch and Flexner,⁸⁴ in which we brought conclusive evidence of the occurrence of pneumoperitonitis without perforation, the first of the kind on record in which similar proof was obtained. Since our publication a similar case has been observed by Dr. Flexner in Manila, who has kindly furnished me the notes. At the autopsy, twelve hours after death, there was found hemorrhagic infarction of the lower part of the ileum and adjacent part of the large intestine, caused by the passage of this part of the intestine through a hole in the mesentery. The peritoneal cavity was greatly distended with gas which burnt with a pale blue flame. There was a large amount of frothy, bloody serum in the peritoneal cavity, together with a fibrinous exudate. The most careful examination showed no perforation. *Bacillus aerogenes capsulatus* was obtained in pure culture and abundantly from the peritoneal fluid. Gas was absent from the blood and other organs.

We have found the gas bacillus, mixed with other bacteria, twice in circumscribed, gas-containing, intraperitoneal abscesses resulting from perforation of the appendix vermiformis.

Hepatic and biliary infections.—The development of gas in the liver is so striking a phenomenon in most autopsies where the gas bacillus and free gas are found in the blood and organs that P. Ernst used the term "Schaumleber" for the title of his article on the gas bacillus, published a year after the paper by Welch and Nuttall, in which we first directed attention to the subject of foamy organs and the gas bacillus.⁸⁵ I have already considered the general subject of gas bubbles in the blood and organs, and wish here to call attention especially to infections of the gall bladder and biliary passages by *Bacillus aerogenes capsulatus*.

In cases of foamy liver gas may be found in the bile ducts and gall bladder, but my experience is that, when the gas bacilli reach the liver through the blood-vessels, the appearance of gas in these situations is a rather late occurrence and met chiefly in advanced cases. In contrast to these cases are the observations of gas in the biliary passages, associated sometimes with definite lesions of the bile ducts and liver, where the evidence is that the gas bacilli entered from the intestine directly into these passages. Two such cases have been reported by Howard⁸⁶ and I have observed 2 cases.

Pratt and Fulton⁸⁷ report a remarkable case of cancer of the common bile duct and pancreas in which cholecystotomy was performed, the opening in the gall bladder being stitched to the abdominal walls. At the autopsy the liver was found studded with minute abscesses with greenish translucent walls. In cover-slips, sections and cultures *Bacillus aerogenes capsulatus* was found in pure culture in these small biliary abscesses, but there was no gas in the abscesses, the liver, blood or other organs. A somewhat similar case, in which cholecystenterostomy for gall stones had been performed, was previously reported by Nicholls⁸⁸ from Adami's laboratory. Here also multiple biliary abscesses containing the gas bacillus were found in the liver, but in this case gas was present in the liver as well as in the blood and other organs, the autopsy being six hours after death. Larkin⁸⁹ has likewise reported a case of hemorrhagic pancreatitis with fat necroses and small, multiple hepatic abscesses with gas holes in the liver, from which *Bacillus aerogenes capsulatus* was isolated. The autopsy was eight hours after death.

Hintze⁹⁰ has recorded a post-mortem observation of gas in the inflamed bile ducts with cholelithiasis. He cultivated only the colon bacillus, but it does not appear that he made anaerobic cultures.

From the foregoing cases it is to be inferred that the gas bacillus may invade the bile ducts and gall bladder from the intestine, and sometimes during life, and that it may not only produce gas but also necroses and purulent inflammation. The presence of gall stones, cancer of the bile ducts and operations on the gall bladder appear to favor this mode of infection.

INTERSTITIAL EMPHYSEMA OF THE GASTRO-INTESTINAL, GENITO-URINARY AND BILIARY TRACTS.

One of the most interesting lesions produced by *Bacillus aerogenes capsulatus* is the formation of submucous or subserous gas cysts or blebs, of which the earliest examples attributed to this organism were reported by P. Ernst, Goebel and Welch and Flexner. They are sufficiently common to have been observed by nearly all investigators who have had much experience with the gas bacillus in human beings. My list of cases includes 25 instances of this condition, of which 5 were of the stomach, 11 of the intestine, far oftener of the small than the large intestine, 5 of the gall bladder and bile ducts, 3 of the urinary bladder, 1 of the renal pelvis, and 1 of the vagina. The majority of the cases were observed by Flexner, Howard and myself, and in all the gas bacillus was demon-

⁸⁰ Canada Lancet, May, 1900.

⁸¹ Boston Medical and Surgical Journal, June 7, 1900, p. 599.

⁸² Welch and Flexner have reported an instance of perforated gastric ulcer causing peritonitis in a rabbit, in which the gas bacillus was found.

⁸³ The purity of the culture in this case is explicable by the results of Cushing and Livingood's interesting bacteriological and experimental studies of the duodenal flora published in Contributions to the Science of Medicine, dedicated by his Pupils to William Henry Welch on the Twenty-fifth Anniversary of his Doctorate, p. 543, Baltimore, 1900.

⁸⁴ Case XIII of our list in Journal of Experimental Medicine, 1896, p. 35.

⁸⁵ Heydenreich's paper on "Emphysem der Leber" (Centralbl. f. Bakt., 1897, xxi, p. 305) may be mentioned as a curiosity. He had never heard of the gas bacillus or of any other investigation of the subject later than 1872. In contrast to this is the interesting article of P. Bernhardt on pneumothorax and foamy organs, with full consideration of the recent literature. Deutsch. med. Woch., 1900, p. 83.

⁸⁶ Contributions to the Science of Medicine, dedicated by his Pupils to William Henry Welch on the Twenty-fifth Anniversary of his Doctorate, pp. 475 and 476, Baltimore, 1900.

⁸⁷ Boston Medical and Surgical Journal, June 7, 1900, p. 599.

⁸⁸ British Medical Journal, 1897, ii, p. 1844.

⁸⁹ Medical Record, 1898, lili, p. 354.

⁹⁰ Münch. med. Woch., 1895, xliii, p. 209.

strated. The case of emphysema of the vagina was reported by Lindenthal.⁹¹

These gas cysts vary in size from microscopic dimensions to large blebs. They are most common in the submucous coat, but may be present in the mucous membrane, the muscular coat, or beneath the serous covering; in fact, in any part of the membranous wall. They may be few or in enormous numbers, in groups or scattered. In one of our cases the whole small intestine from the duodenum to the ileocecal valve was studded with small gas cysts. Gas cysts of the same general character may be found in the mesentery and omenta.

These gas cysts are in their inception simply such gas holes as we are already familiar with in the liver and other organs in cases of local or general invasion with the gas bacillus. They indicate a foamy or emphysematous condition of the walls of the stomach, intestine, gall bladder, bile ducts, urinary bladder and vagina, due to the invasion into these parts of the gas bacillus.

The condition of the walls of the blebs and of the surrounding tissues varies. Some of the cavities are round and their walls smooth, others are irregular in shape and have ragged walls. They may correspond to dilated lymphatics, but more frequently they do not represent dilatation of any preformed channels. There may be communication between adjacent cavities, but oftener the cysts are distinct from each other. The tissue in the immediate neighborhood of the cavities may present no alteration not explicable by the mechanical pressure of the gas, or it may show necrosis in varying degree and extent. Inflammatory changes or cellular reaction which could be reasonably referred to the presence of the cysts or of the gas bacilli causing them were not noted. Sometimes a little coagulated, homogeneous or granular material is present in sections of the cysts in hardened tissues, as indeed may often be found in gas holes in the organs.

In sections stained by Gram there is usually no difficulty in demonstrating the relation of the gas bacilli to the cysts. The bacilli may be in masses in the walls of the cysts, but sometimes they are not more numerous there than in the tissue at a distance from the gas blebs, and occasionally it requires some searching to find them. By anaërobic methods the gas bacillus can be cultivated from the cysts or the adjacent tissue.

All of the instances of submucous and subserous gas cysts in my list were observed post mortem. In the larger number of cases gas bacilli and gas bubbles were more or less widely distributed in the blood and organs, but without evidences of ordinary post-mortem decomposition. There are, however, several cases in which these gas cysts in various situations were the sole manifestation of the presence of the gas bacillus in the body. Howard has shown that if careful systematic search is made for areas of necrosis and minute gas cysts due to *Bacillus aërogenes capsulatus* in the stomach and intestine, these lesions can be found much more frequently than has been supposed.

It is with our present information a difficult matter to say in how many of these cases the emphysematous state existed before death. It is certain that, at least in the great majority of cases in my list, the emphysema was not the result of ordinary post-mortem decomposition. In a large number of the cases the

autopsy was made within a few hours after death. Howard in one of his cases of gas cysts, limited to the intestine, made the autopsy one hour after death. I have already emphasized the importance of great caution in interpreting as vital processes the various gaseous conditions of parts and organs not open to inspection during life, even when autopsies are made soon after death and there is entire absence of putrefaction, and I can only repeat this caution here. Mere absence of nuclear staining around gas holes, I do not regard as proof of their origin during life.

It would lead altogether too far to enter here into a discussion of the general subject of submucous gas cysts, concerning which there is a large literature, the principal references to which will be found in the articles of Eisenlohr,⁹² Camargo,⁹³ Winands,⁹⁴ Dupraz,⁹⁵ and Lindenthal.⁹⁶ It would appear from a study of the records of the subject that anatomically different conditions have been described under the designation "gas cysts" (*cystides aëriferae*). Some have been apparently of long standing and show chronic inflammatory changes in their walls and surrounding tissues. The most voluminous literature relates to the gas cysts of the vagina (*kolpolypertrophia cystica* of Winckel, *emphysema vaginae* of Eppinger).

At present we have no warrant to identify the more chronic gas cysts with thickened walls with the more acute emphysematous condition which I have described as referable to *Bacillus aërogenes capsulatus*. Nevertheless the former are probably of bacterial origin also, although I am unable to accept the bacteriological findings of Eisenlohr, Camargo and Dupraz as at all convincing, for they made no use of anaërobic methods of cultivation. It is quite possible that *Bacillus aërogenes capsulatus* is concerned also in the etiology of the gas cysts of long standing; certainly it is important to apply hereafter anaërobic cultural methods to their study. Lindenthal has no hesitation in identifying the emphysema of the vagina observed by him post mortem and from which in a single case he cultivated what he chooses to call *Bacillus emphysematis vaginae* (in reality our *Bacillus aërogenes capsulatus*) with Winckel's *kolpolypertrophia cystica*, but while he may be correct, further observations are needed before this anatomical and etiological identification can be accepted.

The only instance in which gas cysts of the human intestine have been recognized during the life of the patient is reported by Hahn,⁹⁷ who found them in large number upon opening the abdomen. It is to be regretted that no thorough bacteriological examination of this case was made.

In my original communication on the gas bacillus I ventured the surmise that the bacillus found by E. Fraenkel⁹⁸ in hardened sections from a case of gastritis emphysematosa might be identical with *Bacillus aërogenes capsulatus*, and this suspicion has gained in probability by Goebel's statements based upon an examination of the sections, his work having been done under Fraenkel's supervision.

Notwithstanding an effort at compression, so much space has been occupied in the presentation of the

⁹² Ziegler's Beitrage, 1888, III, p. 101.

⁹³ These de Genève, 1891.

⁹⁴ Ziegler's Beitrage, 1895, xvii, p. 38.

⁹⁵ Arch. de méd. expér., 1897, ix, p. 282.

⁹⁶ Wien. klin. Woch., 1897, pp. 3 and 35.

⁹⁷ Deutsch. med. Woch., 1899, p. 657.

⁹⁸ Virchow's Archiv., 1889, cxviii, p. 526.

⁹¹ Wein. klin. Woch., 1897, pp. 3 and 35.

foregoing subdivisions of our subject, which in less than a decade has grown to considerable magnitude, that I shall only summarize very briefly a few remaining topics, although all deserve fuller treatment.

Pulmonary and pleural infections.—To the two instances of invasion of the lungs by the gas bacillus reported by Welch and Flexner I can add the cultivation of this organism from a gangrenous lung by Dr. Flexner in my laboratory.

Of much importance is Levy's⁹⁹ demonstration of *Bacillus aerogenes capsulatus* as a cause of pneumothorax without perforation. This case and those of pneumoperitonitis without perforation to which I have already referred have settled affirmatively the long standing controversy concerning the possibility of the generation of gas within closed serous sacs during life.

Nicholls¹⁰⁰ has reported an instance of pneumothorax and pneumocardium without perforation, in which the gas bacillus was probably present. Finley¹⁰¹ and May and Gebhart¹⁰² attribute their 2 cases of pneumothorax without perforation to the colon bacillus, but in neither were anaërobic cultures made. It is important in all gaseous affections to search for anaërobies.

Gas bacillus in the blood during life.—Extremely interesting is the demonstration by Gwyn,¹⁰³ both by cover-slip specimens and by cultures, on repeated examinations, of *Bacillus aerogenes capsulatus* during life in the blood of a patient in the Johns Hopkins Hospital, with chorea insanienis and acute endocarditis. I had the opportunity of examining his cultures, which were entirely typical. The patient died, but unfortunately no autopsy could be obtained. There was no evidence during life of free gas in the blood or tissues. The case is of importance as demonstrating that gas bacilli may be in the circulating blood for days in sufficient number to be demonstrable both microscopically and culturally without evidence of free gas. I have already expressed my suspicion that Achalmé's anaërobic bacillus, which has likewise been cultivated from the blood as well as from the tissues of several cases of acute articular rheumatism, is identical with *Bacillus aerogenes capsulatus*.

Presence of the gas bacillus without gas.—In this connection I may say that the gas bacillus may be present and even multiplying within the human body without the production of gas. Certain organs, above all the liver, offer much more favorable pabulum for the generation of gas than do others, but even in the liver the bacilli may be present without gas. I have found gas bacilli in small clumps within the spleen and kidney, surrounded by areas of necrosis, without recognizable gas. I have already cited the demonstrations by Cushing and by Pratt and Fulton of the gas bacillus in small abscesses without gas, the observation of the latter being particularly complete and satisfactory.

Dr. Harris in my laboratory isolated the gas bacillus in pure culture from an abscess containing blood and pus in the neck of a dog, following an operation on the jugular vein. There was no gas in the abscess. Aerobic cultures were entirely negative. These observations, however, are not the only ones demonstrat-

ing that the gas bacillus may under certain circumstances and in certain situations manifest pyogenic capacity.

Meningitis; pyogenic capacity of gas bacillus.—Howard¹⁰⁴ in April, 1899, reported a case of acute fibrinopurulent meningitis, following operation for urethroperineal fistula. *Bacillus aerogenes capsulatus* was found in pure culture in the meningeal exudate. Hirschmann and Lindenthal¹⁰⁵ have recorded another convincing example of acute cerebral meningitis following fracture of the occipital bone, in which the gas bacillus was found unmixed with other bacteria. These authors call attention to the pyogenic power of the gas bacillus when it attacks the meninges, but, as already shown, the same power may be manifested elsewhere.

Cavities in the brain.—Finally, I would call attention to Reuling and Herring's¹⁰⁶ and Howard's studies of cavities in the brain produced by *Bacillus aerogenes capsulatus* and to the light which their observations shed upon certain obscure examples of cerebral cavities previously reported.

In this excursion into pneumatopathology I have invited you to the survey of fields comparatively new and little trodden. I can only hope that our journey has been not without some interest and some profit to you. To me the opportunity to present before such a body as the Massachusetts Medical Society the results of these investigations is one which I highly appreciate.

I desire in closing to pay my tribute of respect and to call to your grateful remembrance the founder of this lectureship, Dr. George Cheyne Shattuck. That the subject of this address would not have been without interest to him may be inferred from the title of his first Boylston Prize dissertation on the theme propounded in 1806 and entitled: "The difference between mortification produced by an external cause and that which is produced by a constitutional defect, the diagnostics and proper mode of treatment of each."¹⁰⁷ By his noble character, professional services and liberality Dr. Shattuck deserved well of the medical profession of his city and State and indeed of the whole country, and his memory is worthily perpetuated not only by the foundation of this lectureship but also by the endowment of the chair of pathological anatomy in the Harvard Medical School.

DURATION OF LIFE IN VARIOUS EMPLOYMENTS.—From the following statistics given in the *Medical Record* it will appear that average longevity apparently has little to do with employment which is not in itself dangerous. A general summary shows that the average duration of life has been about sixty-eight years and eight months. Forty-six poets average sixty-six years, 39 painters and sculptors sixty-six years, 30 musicians sixty-two years, 26 novelists sixty-three years, 40 men of letters sixty-seven years, 22 religious sixty-six years, 35 women sixty-nine years, 18 philosophers sixty-five years, 38 historians sixty-five years, 58 scientists and inventors seventy-two years, 14 agitators sixty-nine years, 48 commanders seventy-one years, 112 statesmen seventy-one years.

⁹⁹ Arch. f. exp. Path. u. Pharm., 1895, xxxv, p. 335.

¹⁰⁰ British Medical Journal, 1897, ii, p. 1844.

¹⁰¹ Philadelphia Monthly Medical Journal, 1899, i, p. 569.

¹⁰² Deutsch. Arch. f. klin. Med., 1898, lxi, p. 323.

¹⁰³ Bulletin of the Johns Hopkins Hospital, 1899, x, p. 134.

¹⁰⁴ Bulletin of the Johns Hopkins Hospital, 1899, x, p. 66.

¹⁰⁵ Sitzungsab. d. k. Akad. d. Wiss., Math.-Naturw. Cl., Wien, 1899, cviii, Heft. 3, Abth. iii, p. 67.

¹⁰⁶ Bulletin of the Johns Hopkins Hospital, 1899, x, p. 62.

¹⁰⁷ Published in Boston in 1808.