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Treatment of lobar pneumonia

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THE TREATMENT OF LOBAR PNEUMONIA

A THESIS

PRESENTED TO THE FACULTY OF
THE COLLEGE OF MEDICINE OF
THE UNIVERSITY OF NEBRASKA
IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF MEDICINE

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TABLE OF CONTENT

Introduction-----page 1.
History and progress of the treatment-----page 3.
Prophylaxis and vaccination-----page 13.
Diet, Fresh air, Diathermy, Drugs, and Oxygen-----page 16.
Serum treatment-----page 26.
Bibliography-----page 36.

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INTRODUCTION.

Among the infectious diseases, pneumonia ranks next to tuberculosis as a cause of death, and in many of our large cities, it kills more persons each year than does tuberculosis. In the public mind pneumonia is generally thought to affect mainly the very young and the old and decrepit. As a matter of fact, over half the cases occur between the ages of 20 and 50 years, during the period of greatest activity.

In the practice of medicine, two questions arise with great frequency; what is the matter with my patient, and how shall I treat his illness? Consequently, diagnosis and treatment are of vital interest to every physician. Of course from the patient's standpoint, proper treatment and the return to normal health is most vital. Often, it is true, pneumonia is diagnosed by the laity, and in some cases, it is treated as successfully by them as by a physician.

It is with this view in mind that the writer has chosen this particular phase, i.e., (The treatment of Acute Lobar Pneumonia) for study.

Although pneumonia was known to the ancients, little advance in the treatment was made until the beginning of the 19th century. Up to a few years ago the problem of preventing the spread of pneumonia or reducing its destructive effects seemed almost hopeless. The fact that bacteria, apparently identical

with those causing pneumonia are found in the mouths of many normal persons seemed to render any proposed measures for the prevention of the infection well-nigh useless.

Hence the writer wishes to correlate and compile, by citing history, and experiments of authorities, the most beneficial therapeutic measures, which scientific medicine has given toward the treatment of lobar pneumonia.

HISTORY.

Pneumonia was known to the ancients, and admirable descriptions of the disease are found in the writings of the great Hippocrates. The general conception was that all painless disorders of the chest were peripneumonia. It was not until the eighteenth century that pneumonia and pleurisy were recognized as distinct maladies. This differentiation dates to the time of Morgagni (1682-1771) who laid the real foundation of modern pathology, and recognized the manifestations of pneumonia to be the result of solidification of the lungs. Baillie (1761-1823) designated the pulmonary change "hepatization" and furnished the ground work for the epochal contribution of Auenbrugger (1722-1809) and Laennec (1781-1826) whose observations led to recognition of the disease by the use of methods of physical (signs) diagnosis and made possible the differentiation of lobar and lobular pneumonia.

From this time until the late nineteenth century no great contribution was made except the elaboration of physical signs and symptoms and better recognition of the disease. In 1874, Von Jurgensen advanced the idea that pneumonia was an infectious disease due to a specific cause, basing his hypothesis largely upon the apparent incongruity between the local lesion and the severity of the systemic manifestations.

Then came the era of bacteriology which proved the validity

of Jurgensen's view.

Friedlander in 1883, recovered organisms from pneumonic exudates and produced experimentally pleuro-pneumonia in mice and guinea pigs. He named this organism, pneumococcus but it was later found to be an encapsulated bacillus and a very rare cause of lobar pneumonia.

In 1880, Sternberg, Surgeon General of United States Army, and Pasteur independently described the organism generally responsible for lobar pneumonia, but neither recognized its specific pathogenic properties. To A. Frankel (1884) this credit is due. He isolated it from the sputum of pneumonic patients, noted its regular presence in pulmonary exudates, and with pure cultures infected, mice, guinea pigs, and rabbits. Later Weichselbaum confirmed his observations.

It was not until the beginning of this century that the path was blazed for the very modern procedures that are modifying our ideas of etiology and epidemiology of the disease and that are furnishing accurate prognostic data and a basis for a specific serum treatment. Neufeld's subdivision of pneumococci into sub-groups are of fundamental importance in the prognosis and treatment of lobar pneumonia.

Thus from his work and the elaboration of workers at the Rockefeller Institute, the disease lobar pneumonia is better understood, more scientifically treated and prevented.

PROGRESS OF THE TREATMENT OF LOBAR PNEUMONIA.

In the year, 1799, mercury in the form of calomel was given

in large doses (30 to 50 grains at a single dose). At that time Sir Thomas Watson said, (the italics are mine) "Many persons, I am persuaded are saved by treatemnt of this kind, pushed to slight ptyalism: the effusion of lymph, tending to spoil the texture of the lung, is arrested and the lymph already effused begins to be absorbed; and the ease and comfort of the patient, as well as the alteration for the better of physical signs, attested the healing qualities of the remedy."

Twenty five years later, Dr. James R. Leaming writes: " I well remember my astonishment when thirty years ago the late Dr. E.P. Cammann ordered a large dose of calomel, in an attack of intercurrent pneumonia in a case of chronic phthisis, and my gratification at seeing the disease successfully controlled thereby. It was perhaps the most practical of all the valuable lessons I recieved from him.----- The admirable sedative effect of calomel when needed is best seen when it is placed dry upon the tongue of the patient.----- The temperature at once begins to fall (italics mine) the heart to gain strength,"etc.-----

The objects of the large doses of mercury were of two folds, namely to reduce the inflammatory condition within the lungs by direct germicidal action through the blood stream, and to produce a sedative effect. According to the reconds given, in no case were they confronted with excessive purging. Stomatitis occurred only twice in fifty cases.

In 1859, Clemens of Frankfort employed the inhalations of

chloroform in pneumonia with a view that it had a sedative action upon the nervous system and also an anti-coagulating(?) effect upon the blood. Here again, the object in view, and the results obtained were due to the supposedly powerful germicide which was brought into direct contact with the consolidation in the lungs, thus killing the invading organisms, and limiting the course of the disease.

Later quinine in large doses, was advocated by many authors suggesting that it had the property of aborting pneumonia by its antipyretic effect. Flint writes: "As long ago as 1861, I was led by the results of the analysis of a considerable number of cases in which sulphate of quinine was given to the extent of only fifteen grains daily, to the conclusion that this remedy exerted a marked curative influence upon the disease. I can now (1881) bear testimony to the fact that, given in larger doses, namely twenty to thirty grains daily, this remedy, in a certain proportion of cases, renders the disease abortive, and that when this does not follow, the disease is often modified to a greater degree than by smaller doses. Now whatever efficacy belongs to these remedies proceeds evidently not from any direct effect upon the pulmonary affection, but from a controlling influence over the pyrexia, thus sustaining the doctrine that the disease is an essential fever."

A.H. Kerr, about this time advocated warmly the use of creosote in large doses in the treatment of pneumonia. He stated: "I do not say that creosote is a specific in pneumonia,

but I do say, and with emphasis, that it is the nearest approach to one that has yet been reached." He dwelt upon its being eliminated largely by the lungs, and thus being brought into direct contact with the lesion. He gave the details of a case seen within twenty-four hours after the chill. The pulse was 120, temperature 104.2 degrees and respirations forty per minute, dulness and fine crepitant rales over the base of the left lung. Ten minims of creosote were given every two hours for the first day with a grain of opium every three hours. Within five days the pulse was 80, temperature 99degrees and respirations normal.

Robert Liegel was the first to introduce the use of salicylates in the treatment of pneumonia. He advocated strongly the use of sodium salicylate in large doses, not less than eight grams daily. From his experience with this drug, he was led to believe that it exerted a specific effect, such as it exhibits in rheumatic fever. Later Dr. A. Ross Matheson substituted ammonium salicylate for the sodium salt. In a letter he wrote to Andrew H. Smith he stated: "I find that ammonium salicylate has some advantages over the soda salt. It is stimulating, while the latter is more or less depressing, and it does not produce to the same extent the throat and ear disturbances. I am satisfied that it has decided value in the treatment of pneumonia."

During the first half of the nineteenth century bloodletting was employed more freely and more indiscriminately in pneumonia, than any other one disease.

Fowler said: "Cyanosis, signs of overdistention of the right side of the heart with epigastric pulsation, and a small irregular pulse are indications for venesection.

The value of oxygen in the treatment of pneumonia was first introduced into this country by Dr. Andrew H. Smith, in 1860. He demonstrated at that time that respirations could be held at a somewhat normal rate, and that cyanosis, could, in part, be prevented. He stressed that oxygen should be ~~resorted to~~ as soon as the respirations exceeded thirty*five per minute or earlier if the lips assumed a dusky hue.

As early as 1888, Netter rendered mice and rabbits immune to pneumonia by injecting them with fluid prepared from the dried spleen of infected animals. Later he experimented with an old pleuritic exudate containing pneumococci, and at last the sputum of a pneumonic patient, which had ceased to be virulent after the crisis.

Pursuing this line of investigation, Foa found that the injection of an attenuated culture of the diplococcus of pneumonia into an animal gave immunity against the disease for several months. He produced the injection serum by precipitating the culture broth containing the diplococci with ammonium sulphate and filtering repeatedly. The filtrate was injected into the veins of rabbits daily for three or four days.

Subsequently he made an extract of the muscles and viscera of a rabbit which had died from pneumonia, precipitated it in the same way, and found that it gave the same immunity.

He next turned his attention to the immune animal, drawing the blood and allowing it to coagulate, when the serum was used to inject another animal. This also gave immunizing results. As a control experiment he injected a rabbit with blood from a man dead of pneumonia; death resulted.

Since the opening of the twentieth century a most intensive study of the immunological problems of the pneumococcus has been carried out with a view to the preparation of a specific serum. It has long been realized that the immune bodies, agglutinins, precipitins, opsonins, and the protective bodies formed in the serum of the immunized animal, are anti-bacterial rather than antitoxic in their action.

Pane, in 1898, reported some measure of success with a serum prepared by immunizing donkeys to the pneumococcus. In 1901, the Klemperer brothers published results with anti-pneumococcus serum prepared in a somewhat different manner. Their report is briefly as follows: Two rabbits were injected each, with 20cc of pleuritic exudate taken from a pneumonia patient and which by culture was shown to be free from living bacteria. Fourteen days later both were inoculated with a virulent culture. Both survived, while the control animal died. Later, they immunized animals with pneumonia sputum taken before the crisis and heated so as to destroy the poison. The same result was obtained by heating to 60 degrees centigrade, a glycerine extract of pneumococci. The bacteria were washed from agar cultures with sterilized glycerine, which was ex-

posed to heat for one or two hours and filtered repeatedly. They found that immunity resulted from doses proportioned in quantity to the strength of the preparation. Later they found that dogs could be immunized against pneumonia, and could also be cured of the disease. From their experiments they concluded that the serum did not kill the organisms present in the system, nor did it prevent their growth, but it acted in one of two ways, either by the preventing the formation of toxin, or by counteracting its effects.

In 1904 Anders concluded from a review of the literature that though the data were insufficient to justify optimism, they were sufficiently suggestive to warrant further investigations.

To Neufeld and Handel belongs the credit for the first preparation of a useful serum. They suggested the need of using large intravenous injections of virulent pneumococci to immunize animals, demonstrated the specific antigenic properties of the several types of the organism and stressed the fact that a proper serum cannot be had for treatment until it is ascertained what particular strain is responsible for the infection in a given case. They also devised a method of standardizing the serum and recommended the intravenous administration of at least 75 c.c.

Dochez and Gillespie isolated numerous strains of pneumococci, and on the basis of specific biologic relationships, established the subdivision of the pneumococcus into

four definite Types, I, II, III, and IV. The immunization of horses by intravenous injections of a given strain led to the production of an antiserum of fair potency against Type I and II and with maximum power of protection against other strains of the homologous type. As yet no satisfactory serum has been prepared for Type III and IV.

In 1921 Huntoon sought to obtain pneumococcus antibodies freed of serum. In doing so, he suspended pneumococci of Types I, II, and III in a large amount of a trivalent serum obtained from horses that had been inoculated with pneumococci of these types. The bacteria, united with the antibodies, were removed by centrifugalization and washed free of serum with saline solution, emulsified in saline solution containing 0.25 per cent of bicarbonate of soda and heated from 30 to 60 minutes at 55 degrees C. The emulsion was then centrifugalized, the supernatant fluid was chilled and filtered through a candle. The filtrate obtained by this method is a clear, colorless fluid and contains only a minimum trace of serum and a high content of antibodies against pneumococcus Type I, and a very little of the antibodies for Type II and III.

Cecil demonstrated that this polyvalent antibody solution had real value in the treatment of pneumonia produced experimentally in monkeys by the injection of pneumococcus Type I, less effect when injected into animals infected with pneumococcus Type II, and no value at all with Type III.

In 1924 Felton discovered that the protective substances in antipneumococcus sera were always contained in the globulin fraction of the serum and that the greatest concentration of them could be obtained in the precipitate that followed dilution of the serum with 15 parts of cool, distilled water. The flocculent precipitate that settled over night in the ice-box was washed again with the same volume of cool, distilled water, and after it had settled once more, the sediment was re-washed, collected by means of a Sharpless centrifuge, dissolved in 0,5 molecular salt solution or tartaric acid, and if the solution was not clear, it was passed through a Berkefeld filter. With this method from 2 and 3 times the concentration of antibodies present in the serum was obtained.

DISCUSSION OF THE TREATMENT OF
LOBAR PNEUMONIA.

PROPHYLAXIS.

A proper discussion of the treatment of pneumonia, begins with a consideration of prophylaxis and the mode of transmission of the disease. It is no longer believed that every healthy person carries a virulent type of the pneumococcus in his upper respiratory tract; nevertheless, it cannot be doubted that many of them act as carriers, especially those in constant contact with pneumonia patients as doctors, nurses and orderlies. In any event the pneumococcus is transmitted from the diseased to the healthy person through the sputum. This being true, one should insist upon the proper destruction of the sputum by heat; paper sputum boxes and paper or gauze napkins should be used freely, changed frequently and then burned. The patient's dishes should be sterilized, and even the bed linen should be boiled. The nurses and attendants should wear proper fitting face masks. A considerable proportion of cases are due to an "auto-infection" due either to a lowering of the host's resistance from exposure to cold, physical fatigue, trauma, the presence of cardio-vascular disease or to an increased virulence of the invading organism.

It therefore becomes necessary for the physician to stress the importance of oral hygiene to a patient convalescing from lobar pneumonia. He should be instructed as to the value

of the frequent use of the tooth brush and antiseptic mouth washes. The public should be instructed in the ordinary rules of hygiene as to the avoidance of overwork, under-feeding, alcoholism and loss of sleep. The civic authorities can aid greatly in the prevention of pneumonia, and all respiratory diseases, by a more rigid enforcement of the anti-spitting law, by proper cleaning the streets, and by systematic disinfection of the rooms in which pneumonia patients have been treated.

Prophylactic vaccination has been advocated by many authors and has in many cases proven successful. Cecil's and Austin's work at Camp Upton, clearly gave evidence that vaccination against Types I, II, and III pneumococci is practical when dealing with an epidemic lobar pneumonia. The only difficulties with which these workers were confronted, were an extreme local reaction, and in a small percentage of the cases, a severe general reaction. It was later demonstrated that if the vaccine was prepared in a lipoid vehicle the severity of the reaction was greatly diminished, and in the majority of the cases nil. In September 1918 Cecil and Vaughan were sent to camp Wheeler to experiment with the lipo-vaccine. 13,460 or 80% of the entire Camp strength were vaccinated against pneumonia with the pneumococcus lipo-vaccine. The dosage in all cases was 1c.c. of the vaccine containing 10 billion each of pneumococcus Types I, II, and III. The local and

general reactions were mild and caused very little inconvenience to those subjected. The weekly incident rate per 1000 men during the period of experiment was twice as high for the unvaccinated recruits as for the vaccinated. Although the results were not as striking as those obtained at Camp Upton by Cecil and Austin, sufficient evidence was produced to justify the use of pneumococcus vaccine when considering bodies of men or children who are exposed to infection, as is the case, either in civil life as in school or colleges or in military life as in camp or barracks or in those in intimate contact with pneumonia patients.

DIET, FRESH AIR, DIATHERMY, DRUGS AND OXYGEN.

Though it is true that pneumonia is a self-limited disease and may terminate happily under the most unfavorable conditions and on the other hand, under the best circumstances, may end fatally, there are few diseases which require more skillful nursing and more intelligent medical supervision. As Cole so succinctly states, the rational treatment of an acute lobar pneumonia has four primary objects in view; first the conservation of the strength and energy of the patient; secondly, the relief of symptoms as they arise; thirdly, the neutralization by non-specific measures of the effects of the disease upon the circulatory and respiratory systems and fourthly, the destruction of the infectious products by specific measures.

DIET.

In the conservation of strength and energy of a patient afflicted with lobar pneumonia, diet, no doubt, becomes one of the most important measures. According to Du Bois, in fever, the average increase of basal metabolism is 13 per cent for each centigrade degree above the normal temperature. Also in fever there is a "negative nitrogen balance" i.e., more nitrogen is eliminated in the excreta than is taken in, in the food. In some cases it is equivalent to a daily loss of from 200--500grams of muscle tissue. This increase in total nitrogen excreted in fever is accompanied by an in-crease

in uric acid, purin bases and creatinin. The increase in purin bodies indicates an increase in the catabolism of the nucleo-proteins of the body; likewise the increase in creatinin indicates destruction of muscle tissue. Any attempt to prevent the nitrogen loss by increasing the amount of protein in the diet, has as a rule, resulted in an increase in the out-put of nitrogen in the urine; however experimental evidence shows that by supporting necessary caloric requirement with carbohydrates, the destruction of body tissues and elimination of nitrogenous materials in the urine, in excess is prevented. The increase in protein metabolism in fever is due to three conditions, namely increase in body temperature, partial starvation from loss of appetite and the resorption of inflammatory exudates. Immediately following the close of the fever, whether it be by crisis or by lysis, there may be an increase in the nitrogenous material in the urine (what is spoken of as the "Epicritical Period") Conversely, during convalescence there are usually a nitrogen retention and a tendency to replacement in the body of the proteins lost during the febrile period.

Litchfield, with the physiology as described in the preceding paragraph in mind, considered that in lobar pneumonia, there are two other important conditions to be met, namely, dehydration and intoxication.----- He therefore advocates strongly the use of glucose in large quantities,

because of its non-toxic and stimulating effect on the mechanism of cell metabolism. Maclachlan and associates, after many years of experience, recommends, particularly in toxic pneumonias, the administration of glucose by mouth (400-600 gms) in lemonade daily, as well as by hypertonic 25% glucose intravenously, 200c.c. four times daily.

In a recent article published in the International Medical Digest, E. Eldon Baum emphasizes the value of glucose therapy in pneumonia. He argues that tissues deprived of oxygen, as is certainly true in pneumonia, live much longer when supplied with sufficient glucose. With his experience, he has concluded that glucose should be administered in small and concentrated quantities, the initial dose being 50c.c. of a 25% solution, which is to be repeated every four hours during the next four or five days and nights, gradually increasing the amount and dilution, until the patient is getting 200c.c. of a twelve and one-half percent solution every four hours.

According to Dr. H. Pratt, in a discussion of the treatment of lobar pneumonia, before the senior class at the University of Nebraska, College of Medicine, the diet should be properly calculated and owing to a defective protein metabolism, the protein intake should not exceed 1gram per kilo of body weight. He considered the metabolism in pneumonia to be increased 20-25 percent and that necessary calories in addition to those required for basal maintenance should be given in the

calculated diet. Thus a patient weighing 150 lbs. or 69 Kilos under ordinary healthy conditions would require only about 69×25 calories or 1725 calories as a maintenance diet. But if the same individual is afflicted with pneumonia the B.M.D. would be increased 20-25% or 2050 calories. The diet should consist mainly of liquids, such as milk, fruit juices to which glucose has been added, and vegetable and beef broths.

It is well known that salt and water are both retained in the tissues during febrile states. This particularly is true in lobar pneumonia and it is more marked in the pneumococcus than in the influenzal pneumonia; the reason for this is not definitely known. However it is definitely known that chlorides administered to a febrile patient, are retained in the body to a greater extent than when given to a normal patient, and it is retained in the tissues, differing from the salt retention of nephritis in that, in the latter the salt is retained in the blood. During the crisis in pneumonia there is an unusual loss of weight due to the elimination of extra water retained. In view of these facts, should salts be restricted from the diet of a patient suffering from lobar pneumonia?

It is obvious that in order to conserve the strength of a patient, they should have complete mental and physical rest. In securing these conditions, a good nurse and the restriction of visitors should be employed.

FRESH AIR.

The fresh air treatment in pneumonia is still in vogue, and according to R.N. Wilson of Philadelphia, it is good treatment, when the diagnosis of lobar pneumonia is absolute and where the patient is showing a normal response to the infection, i.e., (leucocyte, temperature and pulse response). He states that with this treatment, "The respirations become easier, the heart action less labored, sleep comes with less effort and food is taken with some relish when the patient is moved even from the well aired room to the outdoor air. Both the cerebral symptoms (delirium) and the occasional distressing intestinal paresis, seem less likely to occur and are more easily controlled under the out door regime."

DIATHERMY.

For the relief of pain, various local applications have been used since the time the disease was first described. The use of diathermy in the treatment of lobar pneumonia, was suggested by Stewart in 1926. Two years later Binger and Christie treated several hundred cases with the diathermy and concluded that it was the best method of applying heat, if penetration to the deep tissues is desired. They were able to increase the local temperature in the lungs a degree and a half higher than the rectal temperature. In many instances the heat gave relief from pleurisy pains.

In many cases, adhesive strapping of the chest wall has given relief from pain. But from a practical standpoint it has proven detrimental, in that it increases the tendency to shallow breathing and anoxemia. The old fashion dry cupping and the simple mustard leaf still has its advocates. In children, a light well made linseed or flax seed poltice will soothe. In both adults and children the "Pneumonia Jacket" will provide additional warmth and not impede respirations.

DRUGS.

Before the twentieth century, drugs were the doctor's only salvation in the treatment of pneumonia. Practically all drugs of any known therapeutic value, as germicides, cardiac or respiratory stimulants, were used, and according to the writers of the time, many of them gave beneficial results. Today, however only a few are considered beneficial.

For the relief of pleural pain, most authorities agree that an opiate as morphine gr $\frac{1}{4}$, codeine gr $\frac{1}{2}$, administered hypodermically every twelve hours during the height of the plurisy is good treatment.

For the relief of abdominal distension, due to a partial paralysis of the bowel, ^{U. S.}terpentine stupes, enemata and the hypodermic injection of pituitrin $\frac{1}{4}$ c.c. or eserine one fiftieth of a grain may be given. Castor oil one-half oz. given by mouth is advocated by some authors.

For over fifty years quinine has been used in one form

or another in the treatment of pneumonia. Originally as a tonic, later as an antipyretic and more recently as a specific remedy.

The discovery of Morgenroth and Levy in 1911 of ethyl hydrocuprein (optochin) a quinine derivative seemed to ^{give} some promise. It was found to exert a specific bactericidal action on pneumococci in the test tube and experimental pneumococcic septicemia of animals.

Cole speaks of a large series of cases in the Rockefeller Institute with disappointing results.

In 1922, Cohn-Bronner in a review of Optochin in the treatment of pneumonia believed that in a certain proportion of cases the disease may be shortened or even aborted.

According to Campbell Howard the best method of administering optochin is to give the base (niemoquin) in milk in five doses of .3 gram or six doses of 0.25 gram per diem; not to exceed 1.5 grams. In many cases toxic symptoms have resulted, such as blindness, tinnitus, deafness, and amblyopia or amaurosis. Owing to these complications Optochin should be given with extreme precaution.

Bronner prefers a solution of quinine muriate 2.0 and urethane 1.0 in 20c.c. of distilled water, 5c.c. being given intra-muscularly. If the fever does not drop within twenty-four hours, the same dose may be repeated. In 138 cases in which the drug was used as soon after the chill

as possible the mortality was only 6.4 percent as compared with 13.4 per cent in the optochin series.

Digitalis has been used in the treatment of pneumonia for over fifty years and many authors of today favor its use; however a search of the literature fails to reveal any studies which present definite evidence that the use of this drug modifies the mortality of the disease. During the year 1928-29, a committee of the staff of the Bellevue Hospital was elected to study the efficacy of digitalis therapy in pneumonia. From their experiments they concluded that digitalis should not be given routinely in lobar pneumonia.

According to many authors, digitalis is indicated only when heart disease coexists or when auricular fibrillation or some other evidence of serious myocardial change has made its appearance, and then it should be given in doses sufficient to rapidly digitalize the individual. Osler advocates the tincture (1c.c.) three or four times a day, and when signs of weakness of the circulation, makes its appearance, intramuscular injections of one of the digitalis preparations. In the severe conditions the use of strophanthin is often more efficient (gr. 1/100) intramuscularly or intravenously.

Oxygen therapy has become more or less a routine procedure today and its success according to McLeod depends on several factors, namely to get as much gas into the alveoli as possible, to start treatment early before irreparable damage

has been done because of anoxemia, and to maintain administration until cyanosis disappears.

The most effective administration of oxygen began in 1917 when Haldane's apparatus was used in the treatment of acute pulmonary edema of war gas poisoning. Since then, various devices (nasal catheter etc.) have been used. In 1921 Borach and Binger invented a portable oxygen (chamber) tent by which the oxygen could be cooled and regulated. After the use of this apparatus in the treatment of several hundred cases, they concluded that before a definite therapeutic value could be obtained, it was necessary to have the oxygen concentration 30-60 per cent. According to these workers, definite value is evidenced by the disappearance of the cyanosis, slowing of the pulse rate with improvement in quality, slowing of respirations and a decrease in restlessness or delirium. They do not consider this treatment curative but merely supportive i.e., it prolongs the life until such a time as the immunity mechanism is able to accomplish recovery.

In 1900 Neufeld discovered that pneumococci in suspension were dissolved by adding bile to them. Several years later Edwin E. Ziegler demonstrated that the bile salts i.e., sodium taurocholate and glycocholate act upon pneumococci as whole bile and that when given intravenously to patient afflicted with pneumonia they tend to terminate the course

of the disease. From his experiments he concluded that bile salts are not toxic or at least do not produce toxic symptoms, do not prevent antibody action, produce lysis of the pneumococci in vitro by weak solutions (1;25,000), give rise to mild anemia, and produce damaging effects on the veins, completely obliterating them.

In the cases cited in his report he gave increasing dose of bile salts, starting with 1 gram in 20c.c. normal saline and increasing each day 2 or 3grams;also increasing the dilution. The largest dose given was 9 grams in 300 c.c. of N. saline; no toxic symptoms resulted. Following these injections the temperature dropped, pulse became slower and respiration less labored. The only disadvantage which he encountered was the damaging effect on the veins. If this condition could be prevented, bile salt therapy might become extremely advantageous in the treatment of pneumonia. However at the present there is hardly enough experimental evidence to render it practicable.

SPECIFIC THERAPY. (Anti-pneumococcic serum; valuable in Types I and II infection; No value in Types III and IV.)

As was stated in the progress of the treatment of pneumonia, Huntoon in 1921 obtained a filtrate which is a clear, colorless fluid and contains only a minimum trace of serum and a high content of antibodies against pneumococcus Type I and a very little of the antibodies for Types II and III.

Cecil and Larsen treated patients with pneumonia at the Bellevue Hospital with this solution, and noted an appreciable lessening of the mortality of pneumonia due to pneumococcus Type I, especially when the treatment was given within the first four days of the disease. They also noted that following the intravenous injection of this solution, a sharp febrile reaction with a chill, cyanosis and dyspnea occurred in many cases within 20 to 40 minutes. In some cases fatalities occurred following the sharp reaction, thus lessening the value of this treatment. The reaction was considered to be due the foreign protein in the serum. It has been demonstrated that thermal reactions do not occur if no more than 50c.c. of the serum are injected, but the therapeutic effect desired is produced only when 100-150 c.c. are given.

In 1924, Felton carried out a series of laboratory experiments on the isolation and concentration of specific antibodies of the anti-pneumococci sera which led to great

practical results. This preparation contains but a small amount of protein (nitrogen content varying from 8 to 15 mg. per c.c.) is polyvalent to Types I and II and to a less extent to Type III; ^{it} it can be given in small doses with less risk.

The Rockefeller anti-pneumococcus horse serum, specific for Type I pneumococcus pneumonia, as prepared by Cole and Moore has proven to be successful; ^{the} however incidence of thermal reactions, anaphylaxis, and serum sickness has been comparatively high. The anaphylactic reaction occurs within 15 minutes and consists of dyspnea, flushing of the face, cyanosis, cough, urticaria, and restlessness. In such cases the immediate hypodermic injection of .6c.c. of adrenalin (1--1000) or .5mgm. of atrophin sulphate becomes necessary. The thermal reaction, within 20 or 30 minutes and is characterized by chill or chilly sensation, some difficulty in breathing and cyanosis, temperature rises of one to three degrees, and then falls usually to normal, associated with profuse sweating. Cole believes that the too rapid or too cold administration of the serum may be responsible for this reaction. The serum sickness does not occur for several days, (usually 7-14 days after administration) .

In Cole's first series of 23 cases treated with the above serum, 3 deaths occurred; 15 out of the 23 were Type I infection with 1 death or 6.6% mortality.

Most authors consider Felton's concentrated serum to be best of the three described in the preceding paragraphs. Cecil and Plummer state, "There is no more striking clinical effect in the whole domain of specific therapy than that which frequently follows the early administration of Felton's serum in type I pneumonia. The temperature drops rapidly, very much as in a natural crisis, and all signs of toxemia frequently disappear within twenty-four hours after the initiation of treatment. The effect of concentrated serum on pneumococcal septicemia is quite as marked as that of unconcentrated serum. Unless the sepsis is extreme (several hundred colonies to 1 c.c. of blood), pneumococci disappear from the blood stream after one or two injections of serum." IN their investigation with Felton's serum the alternate case method was used; that is, every patient diagnosed as having lobar pneumonia was given a number; the patients with even numbers received the serum, -those with odd numbers served as controls. In most cases they administered from 100,000 to 200,000 units (from 40 to 100cc.) of the serum during the first twenty-four hours of treatment. All together, 239 cases of type I pneumonia were treated in this manner, with a death rate of 20.1 per cent, 234 alternate controls showed a death rate of 31.2 per cent.

Most authors agree that serum treatment in specific types I and II pneumococcal infection, is beyond the experimental

stage and should be employed as early as possible in the course of the disease.

DOSAGE OF FELTON'S ANTI-PNEUMOCOCCUS SERUM.

The serum is standardized to contain between 300, and 2,000 for type I; 100 to 800 units for type II and between 10 to 100 units for type III pneumococci per cc. of serum. A unit being that amount of serum necessary to protect a mouse against .05 cc. of a 1:10 dilution of an 18 hour culture of pneumococci which usually is equivalent to at least one million lethal doses. As has been stated before this poly valent serum is potent for type I but weak for type II, and almost worthless for type III.

According to Avery, results are obtained only when large doses of the anti-pneumococcic serum are given intra-venously in order that a wide distribution of immune bodies throughout the body may occur rapidly. Experiments have shown that not only do the bacteria circulating in the blood, fix antibodies and so render them ineffective, but in the infected patient the blood contains soluble substances which fix antibodies just as do the bacteria themselves. In the severely infected patients these soluble substances may be present in very large amounts, and it is only after these substances are all saturated that an effective concentration of immune bodies in the blood can be obtained. Moreover, it is not only necessary that the desired concentration

of antibodies should be present immediately after the injection, but also that this concentration should be maintained.

The average practice among authors is to give slowly 20cc. intravenously after testing for sensitiveness by the intradermal test. This dose is repeated every eight hours until definite results are obtained.

It has been proposed by many authors, that as soon as a case has been diagnosed as lobar pneumonia, serum treatment should be started; however owing to the high cost of the serum and to the fact that the serum is only valuable in types I and II infections, and these types represent only about forty per cent of the cases, this procedure would be very impracticable. It therefore becomes necessary to make a quick determination of the type of the infection. Avery and his associates at the Rockefeller Institute have proposed a method of quick determination. It is as follows: Select a kernal of sputum the size of a bean, wash and emulsify in broth and inoculate directly into a centrifuge tube containing about 4 cc. of special medium (which is meat infusion broth 0.3 to 0.5 acid to phenolphthalein sterilized by the Arnold Method and containing 5 cc. of steril 20% glucose solution and 5 cc. of steril defibrinated rabbits blood to each cc. of broth) Incubate in water bath at 37 degrees C for five hours, then streak a blood agar

plate with a loopful of culture fluid for isolation of pneumococci in pure culture and the subsequent confirmation of the type. Next remove the red blood cells from the culture medium by slow centrifugation. Then place 3 cc. of the supernatant bacterial suspension in a second centrifuge tube containing about 1cc. of sterile ox bile. Allow to stand in the water bath at 37 degrees C. until solution of the pneumococci bodies has occurred (usually twenty minutes). Then use five tenths cc. portions of the bile solution of pneumococci in precipitin reactions by mixing with an equal volume of immune serum.

By this method, the type of infection may be determined and treatment instituted the same day. According to Avery this method of determination should be used only as an emergency and not as a routine procedure.

SUMMARY.

1. Every physician should stress the importance of prophylactic measures to a patient convalescing from lobar pneumonia.
 2. Prophylactic vaccination is valuable when dealing with large congregations.
 3. Rational treatment of lobar pneumonia consists of , conservation of the strength and energy of the patient, relief of the symptoms as they arise, the neutralization by non-specific measures of the effects of the disease upon the circulatory and respiratory system and the destruction of the infectious products by specific measures.
 4. Diet, fresh air and oxygen conserve the strength of the patient.
 5. Digitalis should not be used routinely. Should be given only when auricular fibrillation or serious myocardial damage coexists.
 6. Optochin has been proven to be valuable, but should be given with extreme precautions.
 7. Poly-valent anti-pneumococcic serum (Felton's) is specific for types I and II, if given in large doses within the first 2 to 4 days of the disease.
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SUMMARY (contd)

8. This serum is practically worthless in types III and IV infection.

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