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The Treatment of Lobar Pneumonia

by

Harley S. Eklund.

1932

Preface

Pneumonia is probably one of the most frequent diseases with which the average physician has to deal. The disease differs from many others in that it is so common and also that its symptoms are quite commonly known among laymen. Therefore, it behooves the doctor, who is called to see a case, to not only be able to recognize the disease but to have at his command therapeutic measures which may bring about a cure of the patient.

Hundreds of different therapeutic measures have been used against the disease and probably no two physicians treat the disease precisely the same. Therefore, to one who is entering into the practice of medicine and to one who has had no personal patients upon whom to exercise his knowledge, it becomes a most difficult problem. Consequently, may the preceding pages cast some light upon the past and present status of the treatment of pneumonia, so that a few general facts may be made a foundation upon which the new physician can institute a treatment which will better his individual patient.

It was my ambition in reviewing the literature to find some experimental evidence upon which the now important therapeutic measures are used. Also, to bring forth such laboratory and clinical data as seem necessary to impress the reader.

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History

Pneumonia is by no means a modern disease. It was recognized by the ancients. According to Howard, (1), the first account was given in the works of Hippocrates (460-370 B.C.). However, it was confused with pleuritis and was called peripneumony. This was disputed by Sprengel who claimed that pleurisy and pneumonia were separate diseases in that pleuritis was an inflammation of the costal pleura while pneumonia was a congestion of the blood vessels of the lung.

Osler, (2), in his textbook quotes Aretaeus' remarkable description, in the first or second century of the Christian era, of the clinical picture of pneumonia. In his description of the symptoms, which were so accurate that even a layman might recognize the disease, he remarks that the cough is dry and may bring up blood tinged sputum. He was the first to describe the blood tinged character of the sputum.

Conrad, (3), found that there was an attempt at distinction between pleuritis and pneumonia down to the time of Sydenham (1695) whose view was generally accepted. Sydenham said; "Having thoroughly considered it only a fever occasioned by a peculiar inflammation of the blood whereby nature throws off the peccant matter upon the pleura, and sometimes upon the lungs whence a peripneumony arises which in my opinion only differs from pleurisy in degree and in respect of the great violence, and the larger extent of the same cause." Wallis in his edition of Sydenham writes: "It has been the custom of almost all authors, when treating of inflammations of the internal parts of the chest, to make a distinction betwixt pleurisy and pneumonia - it is

seldom found but these two affections are united in the same degree. Besides they can scarce ever be distinguished by the symptoms, and to discriminate them would be of little value in practice, in as much as require precisely similar methods and cure."

From Sydenham to Laennac, according to Conrad, (3), peripneumony was the term applied and during this time there was no attempt at differentiation between the two diseases, only to say that peripneumony was the term applied to the more severe form and pleurisy to the less severe form of the disease. The disease as recognized today was made possible by Auenbrugger (1761), and Laennac (1819), who clearly pointed out the percussion and auscultation signs found within the chest.

Howard, (1), related that Mathew Baillie (1793), called attention to the resemblance of the pneumonic lung to the liver (hepatization).. Conrad, (3), says that Rokitansky, (1842), described the minute anatomy of the disease and differentiated it into lobar and lobular varieties.

According to Howard, (1), Louis Pasteur in 1881, isolated the pneumococcus from the sputum and in 1884, Fraenkel determined that this organism was the most frequent cause of pneumonia. About this same time Ruffer demonstrated a gram positive pneumococcus isolated from an Egyptian mummy many thousand years embalmed, showing that the coccus was present many thousand years ago. Neufeld, in 1910, isolated pneumococci into four different groups which was later confirmed by many others.

Ancient Therapy.

As stated by Conrad, (3), Hippocrates treated the disease

quite precisely. For the severe pain in the shoulder and arms, he bled the patient sometimes to the point of syncope. For the pain in the chest, he applied lionseed poultices and used cupping. If they had pain in the abdomen, or lower chest, he purged them withholding food. Up to 1871, bleeding was the principle method of treatment. Walshe, at this time, did not believe in the method so much, but the general opinion forced him to bleed his pneumonia patients. However, the amount of blood letting was a question and subject for debate. It seemed that in the beginning of the disease as much as 24-36 ounces of blood could be let three times a day which seemed to be beneficial to the patient in the early stages of the disease, but in the later stages more caution had to be taken.

Smith, (4), states that during the first half of the nineteenth century blood letting was a common practice. They found that the patient breathed easier and that the pulse lost its hard tense character. The "cupping" of the clot and the "buffy coat" were pointed to as being the urgency for the occasion. It was recorded, in Berne in 1762, that ninety-five cases were treated by this maneuver with eighty-five deaths. Whereas, seventy seven cases were treated without bleeding and only ten were fatal. By the latter part of the nineteenth century bleeding in the early stages of pneumonia had lost its prominence as a therapeutic measure but the value in the late bleeding of some cases was advocated by many. They believed that cyanosis, signs of overdistention of the right side of the heart with epigastric pulsation, prominence of the juglar veins and a small and irregular pulse were indications for venesection, and relief was generally

given when six to eight ounces of blood had been withdrawn.

According to Conrad, (3), at the close of the eighteenth century, blisters were commonly used. They were used on the legs and arms with the idea of exciting the powers of the system, thereby rendering admissable further bleedings. Alkalies were also used. They believed them to be efficient in rendering the blood less plastic. They also knew that when hepaticized lungs were placed in alkaline solutions that the lung tissue softened. Alkalies used were bicarbonate of soda, potassium or ammonium soaps and also potassium or sodium sulphates. They also practiced purging pneumonia patients with the view in mind that they were lessening the congestion in the lungs and rendering the individual less likely to have bilious complications.

Calomel and opium were used either separately or combined. Large doses of calomel, one to five grains were used. Smith, (4), states that in 1850 Watson, Cameron and others used mercury to the point of salivation. Doses ranging from fifty to sixty grains of calomel were given early in the disease believing it to have a sedative action. Tartar emetic was used by some of the physicians to the point of producing vomiting and as high as five to six stools daily. Tonics were given chiefly in the form of wines and barks.

Conrad, (3), relates that about 1859 chloroform inhalations were used chiefly by Varentrapp and Wucherer. Sixty minims of the drug was placed on cotton and the patient was allowed to inhale this every ten to fifteen minutes, not enough to produce unconsciousness. Smith, (4), states that about this same time

Clemens, of Frankfort, used chloroform inhalations describing its sedative action on the nervous system and its anticoagulating effect on the blood. He also described its results to its powerful antigermicidal effect on the organism in the lung.

About 1861 Flint began using quinine in fifteen grain doses daily and concluded that it exerted a marked curative effect on the disease. In 1881 Smith (4) advised twenty to thirty grain doses daily claiming that in these doses it aborted the disease. In 1895 Kerr advocated the use of creosote in large doses. He considered it the nearest approach to a specific in that it was eliminated largely by the lungs. He used it in ten minum doses every two hours. Robinson recommended the value of creosote inhalations not only for benefit of the patient but also for prophylaxis of attendants. Dr. Robert Liegal in 1898 wrote concerning the use of sodium salicylate in large doses such as one hundred twenty grains per day. He treated seventy two cases ranging in age from sixteen to seventy four years without a single death and found that from the second day on the fever gradually disappeared and symptoms abated. He considered this form of treatment to have a specific effect such as it exhibits in rheumatic fever. He assumed that it acted upon the mucous membrane increasing its secretion and thereby throwing off the exudate, as croupous membrane is thrown off from the larynx.

I might state that oxygen therapy is by no means a modern contribution to the treatment of pneumonia. According to Smith, (4), it was introduced by him into this country in 1860. He considered it an important aid in the treatment and a definite

physiological aid to the patient if used early in the disease. The most common error, he believed, was the delay of its use until the patient became cyanotic and the aid hunger became marked. He believed that the use of oxygen would tend to ward off such symptoms if used early in the disease.

Conrad, (3), related that at the beginning of the twentieth century there came the general opinion that drugs seemed not to have much influence on the course of the disease and a frantic search for specifics for the disease started. Many claimed many different drugs to be specifics. Among them was Schwartz who claimed that iodine was a specific. Other drugs which held the reign for short times were soda benzoate, salicylates, ergot, creosote carbonate, and a variety of others. About 1910 serums and vaccines came into prominence.

Prophylaxis.

In recent years prophylaxis has come to be regarded as a primary therapeutic measure in treatment of many diseases. So it is with pneumonia that prophylaxis is an important measure in prevention and spread of the disease. According to Austrian, (5), auto-inoculation seldom is the cause in a case of pneumonia. He says that special research carried on by the Rockefeller institute shows the disease to be more commonly due to infection by contact either direct or indirect. Types I and II, which are responsible for over 60 per cent of the pneumonia cases, are never harbored in the normal buccal cavity but are found only in patients suffering from the disease or in the sputum of convalescents (convalescent carriers), or persons who have

acquired the organisms by being in close contact with pneumonia patients (healthy carriers).

Every case of pneumonia is a possible source of infection, and thus measures as are necessary to prevent spread of other contagious diseases should be used here. The patient should be isolated, all eating utensils, clothing, linens, etc., should be sterilized by boiling before removal from the room. All excreta should be properly sterilized before being disposed of. A 5% phenol solution is a good antiseptic for this purpose. The room should be cleansed daily so as to prevent spread by dust and after convalescence the room should be cleansed preferably with hot soda water and allowed fresh air and sunshine. Attendants and members of the family should by all means carry out prophylactic hygiene and pay especial attention to the throat. Also, it is advisable that they wear a gauze mouth and throat guard. Known carriers should be instructed as to dangers of sneezing and coughing in the presence of others. Howard, (1), states that a considerable proportion of cases are due to auto-inoculation as a result of the lowering of resistance from exposure to cold, physical fatigue, trauma or presence of cardiovascular disease or to increased virulence of the organism.

With reference to specific vaccination, Howard, (1), states that as early as 1913 Lister working among miners in South Africa vaccinated a large group of workers with large doses of killed cultures at seven day intervals and proved to his satisfaction that immunity was established for a period of one year. Later Cecil and Austin working at Camp Upton inoculated more than 12,000 soldiers. Cultures were made by growing in 0.5% glucose broth,

and killed by heating to 53°C. for half an hour. Types I, II, and III pneumococci were used, and the inoculations made at 3-7 day intervals. They obtained fewer local and toxic reactions following the use of repeated small injections. Total dosage was six to nine billion of Types I and II, and four to six billion of Type III. Over a period of ten weeks observation not a single man developed pneumonia ^{who} which had been vaccinated whereas in a control group of 20,000 men there were 26 cases of pneumonia due to types I, II and III pneumococcus.

Cecil (6), states that prevention of pneumonia means the prevention of the milder respiratory infections. Nearly every case in the Bellevue Hospital gives a history of a previous sore throat, cold or influenza. He is convinced that with respect to the common cold that autogenous vaccines every week or ten days throughout the spring and winter are of great value in their prevention. He advocates the use of a polyvalent vaccine for patients who have had several attacks of pneumonia and live in constant dread of still another attack. Pneumococcus vaccine is indicated also in elderly patients who suffer every winter from bronchitis. It is a prophylactic measure against the more serious complications.

General Management.

As in many other diseases rest is a primary and essential factor in the treatment of pneumonia. As clearly pointed out by Howard, (1), a suitable bed should be provided with a firm spring mattress so that the patient acquires the greatest relaxation. An adjustable headrest is an advantage in that the patient can be placed in the semi-Fowler position so that the

greatest relief from dyspnea can be obtained. Too frequent examination of the chest should be refrained from, visitors should be limited to numbersⁱⁿ and visits made short. According to Austrian, (5), daily examinations of the chest, especially the posterior lobes, should be made, because only in this way may the extent of the pulmonic lesion be noted and the chance for overlooking a pleural exudate^{be} is minimized. No unnecessary exposure or exertion should be allowed. The patient should not be allowed to sit up at any time.

The majority of men advocate treating the pneumonia patient by allowing plenty of fresh air. A temperature of 60⁰F. is not unharmed and seems to have a distinct advantage in comforting the patient. Austrian, (5), says that the windows should be open and whenever conditions allow the patient should be wheeled on to a protected porch. Fresh air makes respiration easier, stimulates the circulation and quiets the nervous system, promotes appetite and, according to statistics, lowers the mortality of the disease. Howard, (1) claims that common sense should be used in allowing the patient fresh air. Undue exposure in stormy weather is absolutely harmful and if the patient prefers being in a warmer room he should be so allowed. R.G. Freeman is a strong advocate of open air treatment and claims it increases the child's vitality so that the disease runs a shorter course, and that the mortality rate is lowered. According to R.N. Willson of Philadelphia; "The respiration becomes easier, the heart action less labored, sleep comes with less effort and food is taken with some relish when the patient is removed even from the well aired room to the outdoor air. Both the cerebral symp-

toms (delirium) and the occasional distressing intestinal paralysis, seem less likely to occur and are more easily controlled under the outdoor regime."

It is generally agreed, that the diet should consist of plenty of liquid, meat and vegetable broths, cereals, egg nogs, soft eggs, custards and jellies. These foods furnish a high percentage of calories and are easily digestible. To increase the calorie content, lactose or glucose may be added to the liquids. Austrian, (5), relates that studies reported by Austrian indicate that in the usual diet of the pneumonia patient there is too little salt. He advocates giving the patient at least 10-25 grams of sodium chloride each day. A copious intake of water should be administered, at least three liters per day because of its effect to promote elimination.

Hydrotherapeutic measures should be taken. The patient should be bathed frequently with tepid water and a brisk rub follow. This promotes circulation, increases blood pressure, stimulates the respiration and promotes elimination. Ice and cold sponging are distinctly harmful and should be avoided.

Pleurisy is such a frequent complication of pneumonia that its treatment really becomes a part of the treatment of the disease. The pain, which is severe, is usually relieved on rendering the chest immobile, and so it is that the physician first thinks of adhesive tape. According to Howard, (1), this is not a good measure since it interferes with chest expansion, promotes anoxemia, interferes with chest examinations and may cause local skin infection. He advocates the use of ice bag or hot water bottle. According to Gordon, (7), the only object in applications to the chest is relief of pain or of an irritating

cough. Ice sometimes works wonders. Strange to say, a hot water bottle or an electric pad may do just the same, though neither has any effect on the progress of the disease. A linseed poultice may succeed where all of the others fail, or vice versa, and a mustard plaster has been a great source of comfort. The use of diathermy has, with some, acquired some popularity.

Tympanites, which often accompanies pneumonia, is regarded by many as a serious prognostic sign. Gordon, (7), claims that its recognition, as a result of toxæmia and not as due to intestinal fermentation, suggests more active hydrotherapy and central nervous stimulation as well as the guarded use of pituitrin. According to Thomas, (9), meteorism is due to splanchnic paralysis and he also regards it as a grave symptom. The abdomen becomes distended, drum-like and further increases the already labored respiration. He advocates the use of surgical pituitrin in doses of $\frac{1}{2}$ -1 cc. Howard, (1), also regards the distension as due to a paralysis of the intestinal musculature. He advocates turpentine stupes; if ^{the patient is} seen early, ^{this} may relieve the patient. If seen late, it may be necessary to give the patient turpentine enema, and if all measures fail he advocates use of pituitrin in 1 c.c. dose hypodermically.

Bleeding, although practiced by the ancients, still has many advocates. Austrian (5), believes that it should be used in all cases where evidence of acute dilatation of the right side of the heart develops, and he advocates the bleeding of 250-500 c.c. of blood. Osler (2) says that in healthy, robust individuals where the disease has a quick onset with high fever and other pronounced symptoms that early bleeding is of value. He definitely states that it is indicated in cases where dili-

tation of the heart occurs. The amount depending on the effect.

Narcotics.

Opium or its derivatives have long been regarded as the most helpful drug in the treatment of this disease, as regards relief from pain and promotion of rest. It is equally beneficial in slowing respiration and also in deepening it. Under opium, in medicinal doses, the minute volume of inspired air is not diminished. Gordon, (7), says that the unfortunate (or fortunate) susceptibility of some people to the drug compels one to try various forms, and where morphia is not tolerated, Dover's powder, or pantopon may be. But in the majority of instances morphia hypodermically is the best form of administration.

Davis, (8), made important observations on the treatment of pneumonia cases with morphine. Older writers were of the opinion that morphine was harmful and only used codiene. Cecile and Cole are of the opinion that morphine should be used for the pain. Davis agrees with Cushny that in cases where the respiration is barely sufficient to aerate the blood, or where profuse expectoration is present, morphine is dangerous, because of its depressant action on the respiratory center, the tendency to abdominal distention, and to the relaxation of the bronchial musculature and thus danger of edema of the lung is increased.

He made observations on human beings, the greater number who were acutely ill with lobar pneumonia. "One hundred and seventy-three observations were made on thirty-three different cases of pneumonia. On these forty-three arterial punctures were made. Fifteen patients were studied in a body plethysmograph from fifty minutes to one and one half hours. An arterial

puncture was done before and after each respiratory tracing was made. Morphine was given subcutaneously while the patient was in the plethysmograph and a second tracing was made from 15 - 30 minutes after the administration of the drug. The dose of morphine varied from 10-18 mgms. The respiratory movements of fifteen patients were studied in the plethysmograph before and after morphine administration. In all but one case there was a drop in rate. The average drop in fourteen cases was 4.1 to a minute. The greatest fall was from 42.5 - 34.4. In one patient the rate increased from 40-42 per minute. His tidal air, however, fell from 244 to 186 c.c. and his minute volume from 9.78 - 7.81 liters. His breathing indicated edema of the lungs and at the time of observation he was rapidly growing worse. His arterial saturation dropped from 85.9-84.7 per cent after administration of morphine."

"The effect of morphine on the oxygen saturation of the arterial blood as observed in 16 patients out of 20 on whom oxygen analysis of the arterial blood ^{was} were done before and after morphine, ~~there was a drop in~~ ^{to lower} the arterial saturation. The greatest drop was 21.3% and the average drop 5%. Of the remaining 4 cases, 3 showed a slight rise in oxygen saturation after morphine. One of these three cases had severe pain, which was relieved by morphine. His tidal air increased from 412-438 c.c. though his minute volume dropped from 13.35 - 10.96 liters. In only 3 cases was the change in oxygen saturation great enough to be of significance. In one the saturation fell from 82.5-64.9. This was a man 63 years of age who had been sick for three days. He appeared cyanotic and dyspneic, signs of consolidation

extended from the left apex to the base. At the left base were signs of fluid. Moist rales were present in both lungs. His blood culture, ^{was} positive for pneumococcus type III. In another case the saturation fell from 87.2-78.7. This was in an obese woman of 50 years who had a severe chill three days previously. The right middle and lower lobes were involved. Throughout both lungs bronchovesicular breathing and numerous rales were heard. She appeared cyanotic. Blood culture was positive for type II. The next day her arterial saturation was 93.2. Five days later she died." He concluded; "In most cases of pneumonia the effect of morphine on the respiratory movements and on the arterial oxygen saturation is slight. Certainly the depression of respiration which follows morphine administration is ordinarily not sufficient to contraindicate its use. The benefits which may accrue to the patient in the direction of relief from pain, reduction of metabolism and sleep, undoubtedly outweigh the possible ill effects of a slight reduction in pulmonary ventilation and increase of anoxemia. Occasionally, however, morphine may so diminish pulmonary ventilation as to result in serious oxygen want. This is liable to occur in patients in whom the pulmonary involvement is extensive and is accompanied by diffuse moisture, and in patients who are already suffering from severe want. Because of the possibility of this type of reaction to it, morphine must always be used with caution and is best combined with oxygen therapy. When there is much pleuritic pain, the relief brought by morphine may allow the pulmonary ventilation to increase and thus raise slightly the per cent saturation of the arterial blood."

Howard, (1), is emphatic in his belief that the best way

to relieve pleural pain is by administration of morphine (gr 1/4), codein (gr $\frac{1}{2}$), heroin (gr 1/12), or pantopon (minums 7) administered hypodermically every twelve hours.

Digitalis

Digitalis therapy has probably been argued more than any other measure in the therapy of pneumonia. Howard, (1), states that it should not be used except when there is coexisting heart disease as auricular fibrillation, or where some other serious myocardial disease coexists with pneumonia. When given it should be given in full physiological dosage so as to get the patient digitalized. This may be done by giving the patient 4 c.c. of the tincture every four hours until six doses have been given, or toxic symptoms of digitalis are brought on.

Niles and Wyckoff, (10), studied 835 cases at the Bellevue Hospital over a period of two years using a control group. They found the mortality to be 7-10% higher in the digitalized group. These cases were studied as to weight, sex and age of patient. They concluded that, although they would like to study the effects of digitalis over a series of years, the committee were of the opinion, judging from effects thus far, that digitalis should not be used in lobar pneumonia patients. Stone, (11), studying a series of 1205 cases of pneumonia and 259 autopsies found that in the autopsies performed, the heart was normal in 20.6 per cent,^{showed} parenchymatous degeneration in 52.9 per cent, fatty degeneration in 11.7 per cent, leukocyte and round cell infiltration in 8.9 per cent,^{and} hyaline degeneration in 2.9 per cent. He believed digitalis therapy to be rational. If it was to be used he believed it should be used early before the

heart had become incompetent through dilatation or muscle degeneration with consequent exhaustion of its reserve toxicity.

Osler (2) advises that only in severe cases should digitalis be administered early. It may then be given in the form of tincture (MXV) three or four times daily. If signs of cardiac weakness become manifest, injections of one of the digitalis preparations is indicated, **Straphanthin** (gr 1/100) intramuscularly or intravenously. Austrian (5), has a similar view in that he believes digitalis in small dosage should be administered early to all pneumonia patients so that if its indications arise a prompt effect can soon be obtained.

Stimulants.

Heart stimulants seem to be commonly employed and have a distinct indication in collapse due to circulatory failure. However in collapse without evidence of cardiac failure Gordon (7) feels that adrenalin and atropin hypodermically have the best chance of restoring vasomotor control. He believes strychnine has gone out of fashion but its use has always seemed rational on account of its known effect upon the spinal centers. Caffeine is undoubtedly a useful cardiac and a respiratory stimulant, but it has the disadvantage of keeping the patient awake. Austrian, (5), and Osler, (2), both support the view that atropin is valuable and should be administered where there is evidence of pulmonary edema. Osler, (2), advocates also the use of strychnine because of its effect on the respiratory center, also that it should be administered only over brief periods in full doses (gr 1/20) every 2 or 3 hours.

Glucose Therapy.

In recent years, probably more research work has been carried on with glucose therapy in connection with a wide variety of diseases. So it is with pneumonia in which case glucose therapy has many sound advocates. Litchfield (12) relates that three-fifths of the body weight is water and the body needs it in order to maintain the volume of blood necessary for the mechanical efficiency of the circulatory apparatus, to carry nourishment to the cells, to carry away soluble waste products of metabolism and to maintain the proper solutions and osmotic conditions essential to normal cell life. When water is taken from blood it is taken from tissues thereby infringing on vital processes of the cells. In pneumonia, besides dehydration we have to deal with intoxication and nitrogen starvation. Hypertonic glucose is a remedy because it is non-toxic, it is quickly utilized by the organism, it is the best sparer of nitrogen, it is a stimulant to the mechanism of cell metabolism and it is easily obtainable and easily prepared.

For clinical work 250 c.c. of a 25 per cent solution is the type used by Litchfield, (12). He uses double distilled sterile water with glucose dissolved, and allows it to flow freely into the vein. Temperature of the solution should be 100°F. He has given as high as 1700 c.c. taking eleven hours without any evidence of glycosuria. He claims that often in glucose administration the patient becomes brighter and less toxic. The respiration becomes slower, the pulse becomes stronger^{and} slower, and the blood pressure rises. The pulse amplitude is increased, ~~the~~ tongue becomes moist, ^{the} patient asks for water and food, the kidneys and bowels become more active. If the patient was restless

or delirious he becomes quiet and goes to sleep, often while the injection is being given. He advocates the giving of glucose at intervals of 8-12-18 and 24 hours as the case may be.

Baum (13) says that the chief problem is how to give a therapeutic amount without taxing a heart muscle which is already overburdened. He advocates the use of small, frequent doses, using an initial dose of 50 c.c. of a 25 per cent solution given with a large syringe and a 22 guage intravenous needle, taking 30 minutes to administer it. This procedure is repeated at approximately four hour intervals during the next four or five days and nights, gradually increasing the amount and dilution until the patient is getting 200 c.c. of a twelve and one-half per cent solution at four hour intervals. He says that sclerosis often occurs at the site of injection and thus new veins have to be used.

Baum (13) explains the probable mode of action of glucose physiologically in that the muscle tissues, including the heart and liver have the power of converting glucose to glucogen and visa versa as the body may need it. Glucose is already partially oxidized and readily assimilable, but must be first converted to glycogen before it can be utilized by the tissues. In this process of furnishing energy for various decompositions and bodily activities, it is reduced to alcohol, carbon dioxide, fatty acids and water. Tissues which are deprived of oxygen live much longer when supplied by glucose. Thus in a patient suffering with pneumonia, having much of the lung generating space filled with exudate, the blood stream filled with toxic products which interferes with oxygen combining power, and a

sluggish heart also deprived of oxygen and glucose, glucose probably gives to the tissues that which will tide them over the crisis.

Baum states, "In health, it is possible for the animal body to synthesize glycogen from carbohydrates, proteins, and to a slight degree from fats. It is also possible for the animal organism to synthesize glycogen from various amino acids as glycocoll, alanine, aspartic acid, glutamic acid and tyrosine. This synthesis is, at least, in part, performed by the liver after the deaminization of the amino acids in the intestinal wall before being carried to the liver in the portal circulation. Here, again oxygen is a prerequisite for this transformation. It is logical to assume, that because of the anoxemia of pneumonia, the stored glycogen is soon depleted and unable to be replenished by the liver and muscle tissues. Another possible assumption is that, the liver, in endeavoring to free the organism of toxemia, puts its function of detoxification to the fore at the expense of its glycogenic function. Koster and others have shown that the administration of glucose causes marked changes in the Kupfer cells of the liver and attribute the beneficial results from glucose to the stimulation of the reticulo-endothelial system." He explains the clearing of the cyanosis on the basis of liberation of carbon dioxide from the metabolism of glucose which acts as a respiratory stimulus. Also, that the kidney function is improved probably by glucose metabolism, the waste products are better prepared for excretion by the kidneys, or that the output is due to a higher intake of liquid.

Mac Lachlan, Kastlin and Lynch, (14), advise giving 400-600

grams of dextrose by mouth per day. They dissolve 200 grams of dextrose (Dextrose powder - Corn Products Co.) in 1000 c.c. of water to which is added the juice of two or three lemons. The liter thus contains about 800 calories and they try to have the patient drink two or three liters every twenty four hours, thus providing 1600 to 2400 calories. When the case is markedly toxic, or will not take enough by mouth, they advise giving 200 c.c. of a 25 per cent solution intravenously taking one half hour for injection. By this method 800 to 1200 calories are provided the patient in 24 hours. A 50% solution however may be used. The adequate dosage by mouth is 400 grams, by vein 200 grams and the closer one gets to 2400 calories per day the better. They advocate that subcutaneous administration is of value where absolutely needed but that it disturbs the patient too much and by rectum they do not get enough calories.

Drugs

Many drugs have held the reign as a specific for the treatment of pneumonia in the search for an ideal specific. Austrian (5), relates that guaiacol carbonate, camphor, creosote, quinine, the iodides, antimony, the salicylates, digitalis, iron and numerous other preparations each have been advocated. None of these have had a specific effect but some may have a curative value. Bridges, (15), ascribes good success with the use of guaiacol carbonate as a routine measure. He advocates using guaiacol carbonate grains 5, quinine grains 2, and strychnin sulphate gr 1/30 every four hours.

According to Howard, (1), quinine has been used for over fifty years. It was used originally as a tonic, later as an antipyretic and more recently as a specific. In 1911, Morgenroth

and Levy discovered ethylhydrocuprein (optochin), a quinine derivative. It was found to exert a specific influence on the pneumococcus in animal experiments. Shortly after Morgenroth made his publication of his discovery, the drug was placed on the market under the trade name optochin. When it was first used, many patients became deaf, ^{had} tinnitis, ^u ambliopic, etc., due to the fact that its proper dosage could not be determined. Prior to 1916, the upper limit of dosage seemed to be 1.5 grams per 24 hours in an average sized man.

Moore and Chesney, (16), found, from the literature they collected, 787 cases treated with optochin with a mortality of 12.96 per cent, a figure which is encouraging. It seems logical that if optochin can be administered in such dosage as to produce within the human organism a condition whereby pneumococci are destroyed in situ or, at least prevented from local or general migration, and from establishment of their growth in previously uninfected regions, it seems ~~unlikely~~ that marked therapeutic results can be expected from its use.

Wright was the first to show that serum from human patients receiving the drug by mouth destroyed pneumococci in the test tube. Moore and Chesney, (16), showed that this action from a single dose lasts but a few hours. The organisms must receive frequent adequate dosages in order to be ~~of benefit~~ ^{destroyed}. They found that the best bacteriocidal action was gotten by giving 0.022 to 0.0268 grams per kilo. of body weight in twenty four hours.

A review of the literature in which cases have been treated seems to give disappointing results in that the mortality is not seriously affected. It may be due to the organisms becoming ^{e.} fast, but since the serum of patients receiving ~~receiving~~ optochin in ther-

apeutic dosage tends to inhibit or in some cases destroy the pneumococcus, it tends to throw suspicion on this theory. Another theory is that the organisms in the blood stream are usually destroyed or inhibited in twenty four hours at most, but that the exudate in the lungs guard the organisms so that the drug does not get to them. The bacteriocidal actions of the drug in the blood serum seems to be very transient. Also, it is a dangerous drug in that toxic symptoms such as mentioned above may occur and even permanent impairment of vision. ^{result.}

Murphy, (17), has recently published an article in which he attributes marked results with the use of intravenous collosol iodine. He uses 10 c.c. of a 1 per cent solution which he repeats if necessary at the end of one or two days. He has only used it on a very limited number of cases in conjunction with the usual routine, symptomatic treatment. He finds that frequently the general toxemia is overcome within twenty four to forty eight hours after the initial dose has been given. Also he attributes marked results with its use in the treatment of post-operative pneumonia.

In reviewing the literature I found that there are still many who routinely advise the giving of large doses of salicylates. Swensen, (18), advises giving full doses of salicylates, usually starting with acetyl salicylic acid, if the patient is able to take it orally. In an adult he used about fifteen grains every two or three hours. If he is unable to take the salicylate by mouth, sodium salicylate is given intravenously or in two to four gram doses rectally, repeating as often as indicated. Along with this type of treatment it is generally agreed that

alkalies should be used to maintain the alkalinity of the blood. Larder, (19), advises that there is nothing better for this purpose than sodium citrate or acetate, 20 grains given every two to four hours as needed. Since the effect is evanescent he maintains that a dose or two should be given during the night. Other alkalies have been used and still are being used such as bicarbonate of soda and potassium citrate.

Oxygen Therapy.

Probably one of the best measures to offer comfort to the patient is the administration of oxygen. As stated previously, its use was first introduced into this country ~~was~~ in 1860. According to Collins, (20), the first article published on the administration of oxygen was in 1887 by George E. Holtzapfle. The patient was given oxygen ~~by being~~ manufactured ^{at} bedside by using black oxide of manganese and chlorate of potash. The man's breathing decreased from 80 to 60 and cyanosis disappeared. The man finally recovered.

According to Cuthbertson, (21), the blood in normal persons is about 95% saturated. If this gets down to 80 or below ~~there~~ ~~are~~ very prominent symptoms arise as are seen in pneumonia patients such as cyanosis, delirium, abnormal irritation of medullary centers and further impairment of the myocardium. Many theories as to the production of cyanosis have been expounded. Cuthbertson believes that the most logical theory is that it is due to a layer of fluid between the air space and alveolar wall or to a functional disturbance of the alveolar epithelium. He believes oxygen is absolutely essential since there is no appreciable diminution in the oxygen capacity or in the power of the blood to become saturated. Also that oxygen is not merely

palliative but curative, and it must be administered at once if it is to break the vicious circle before the onset of untoward symptoms.

Oxygen is transmitted by the blood in^a combination with hemoglobin called oxyhemoglobin and is dissociated from the hemoglobin as is needed by the tissues in their metabolism. As the oxyhemoglobin loses its oxygen it loses its bright red color and becomes increasingly darker. It is the reduced^{oxy} hemoglobin which gives the blood its peculiar color in pneumonia and accounts for the cyanosis seen in most cases of pneumonia. When there is a large amount of reduced^{oxy} hemoglobin in the blood we are in the habit of speaking of this^{condition} as anoxemia. There is a definite amount of oxygen that a hemoglobin molecule can take up and this is in definite proportion to the iron content. The percentage saturation is of great value in pneumonia. If an artery is punctured we can determine the oxygen content and the maximum amount of oxygen this amount of blood will take up. The ratio between the first and the second figure is known as the percentage saturation of the hemoglobin. Normally the oxygen content is 19 volumes per cent so that the per cent saturation is 95 per cent. It is known that anoxemia may get marked in pneumonia and it has been shown that it bears a relationship to the mortality. A hemoglobin percentage saturation less than 70 per cent indicates a grave prognosis.

Guedel, Shiner and Cunningham, (22), say that for each degree of fever reaction there is an increase of 7 per cent in the metabolism so that the tissues are burned much faster. This puts a strain on the cardio vascular system by calling for an increase

of oxygen to the tissues to support the increased metabolism and more food to carry on the work.

Quoting Guedel, Shiner and Cunningham:- "As engorgement progresses to consolidation the pulmonary absorption area may be decreased to the extent that sufficient oxygen for the support of the increased metabolism cannot be delivered into the blood stream from an ordinary atmospheric environment. The patient early develops a pleuritis, the pain of which, through the physical and mental excitement that it provokes, further increases the body metabolism. The patient manifests the anxious restlessness of air hunger early, with the pleuritic pain inhibiting a fuller respiratory excursion to supply the additional air that is needed. This restlessness is another potent factor in increasing body metabolism. Thus, with the arterial oxygen low and the metabolic oxygen high, nature reacts by increasing the cardiac output to compensate for the increasing oxygen unsaturation of the blood and body tissues."

"Physiology depends largely on oxygen for its support. Any oxygen deprivation interferes with the complete combustion of the body wastes with the inevitable resultant dysfunction of cell acidosis. An acidotic cell cannot utilize the food that is carried to it."

"Dextrose furnishes largely the power by which muscle contracts and by which the body carries on. In the execution of this power, through chemical combinations or reactions dextrose is converted into lactic acid. In the conversion of dextrose to lactic acid oxygen is not required. However, whereas probably five parts of dextrose are thus converted into lactic acid through muscle work, four parts of this lactic acid are reconverted into

dextrose, to be used again in the repetition of the same process. This reversion is notably an oxidation reaction. The remaining fifth part of lactic acid is further converted by oxidation into carbon dioxide and water, in which form it is eliminated. Any interference with the reversion of lactic acid into dextrose will necessarily rob the body tissues of their sustenance. In pneumonia, such interference is in proportion to the degree of anoxemia present. Also, the same oxygen depletion, by its failure to support the reversion of lactic acid into dextrose, will leave deposited within the cell proportionately more waste lactic acid, which cannot be eliminated. Thus in prolonged partial anoxemia a vicious circle is formed. Assimilation of foods is inhibited because of cell acidosis, and cell acidosis cannot be relieved without oxygen. There is an ever increasing demand for oxygen with a progressively decreasing oxygen supply. Therefore nature continues to impose more work on the heart in an effort to provide a compensatory increase of blood to the cell. It must be remembered, the heart muscle, which is called on to do more work is also suffering as are the other tissues. If the antibody defense is raised to sufficient power to neutralize the toxins of the invading pneumococci before the heart must collapse, recovery is most assured. In pneumonia the immediate problem is the heart. The general problem is the maintenance of physiologic function."

By elevating the partial pressure of oxygen in the atmosphere we increase the rate of absorption through the alveolar epithelium. Too many errors are made by administering oxygen too late. Early application is advised ^{since} ~~that is~~ as soon as the respiratory rate can be lowered ^{as} the patient ^{becomes} ~~made to be~~ less

restless and more comfortable. It is easier to maintain a normal physiologic state than it is to retrieve it when it is lowered by intoxication and malnutrition.

The diffusion rate depends on the partial pressure of gases on opposite sides of the membrane and on the permeability of that membrane. A 20 per cent oxygen in atmospheric pressure is adequate to maintain ample diffusion through the normal alveolar membrane. In pneumonia the inflammatory engorgement and exudate renders a much larger area less permeable than does the actual consolidation so it becomes necessary to increase the atmospheric oxygen pressure to maintain normal diffusion.

A dosage of 30 to 50 per cent is adequate to eliminate the anoxemia factor. This should be given as soon as specified previously and kept up until well after the crisis when all symptoms of anoxemia are abolished. The exact dosage is regulated by the symptoms. One may adopt the slogan; "Keep the finger-nails pink."

The patient should be made to understand it is only a therapeutic measure and not a last resort, as the public are of the opinion that it is the last resort to prevent death. Quoting Guedel, Shiner and Cunningham, (22), "Oxygen therapy in pneumonia to the abolition of anoxemia accomplishes the following, It provides a higher oxygen saturation of the blood and thus lessens the heart load. It supports the functions of waste combustion and cell nutrition. It supports the aerobic stage of muscle work (reconversion of lactic acid into glucose) and thus conserves food resources. Finally the cell having less lactic acid thrust on it and having oxygen support for the combustion

of that which it must eliminate, is kept in a more nearly normal physiologic state. The same is true of the heart. Its fatigue products are better carried off, its cells are better nourished, and its work is less. Under ample oxygen support the pneumonic heart, as well as the entire human organism, carries on better and longer than would be possible under partial anoxemia. A few hours or days added to the resistance period contributes that much more time for completion of the antibody defense. Finally, the intelligent administration of oxygen in pneumonia is physiologically sound. Although it cannot constitute an entire treatment, it is an important therapeutic measure."

Collins, (20), treated nineteen cases with the oxygen test. The time at which this treatment was administered he did not say, however he noted that in every case except one the cyanosis was relieved and the patient became less restless and breathed more easily.

Personally, I am acquainted with one case in which the oxygen test was used with marked success in comforting the patient as shown by less rapid and labored respirations, less restlessness and disappearance of cyanosis. This was a woman, aged 31 years, white, married, who entered the University Hospital February 11, 1932 complaining of pain in lower abdomen, difficult, rapid respirations, and productive cough. At this time she was seven months pregnant. She gave a history of having had grippe, accompanied by cough, three weeks previous to entrance. Three days previous to entrance, her respirations became rapid and painful. Her history was essentially negative except that the patient had not menstruated since June 6, 1931. Family history was negative.

Temperature on entrance was 105°, pulse 140 and respirations 48. Face was flushed and lips cyanotic. Examination of chest revealed dullness on percussion over entire right lung and over left base. Bronchial breathing, and five rales were heard at the end of inspiration over the same area. Abdominal examination revealed that she was probably seven months pregnant. Urine analysis at this time was negative. Blood count was 4,800,000 red cells, 23,800 white cells. Differential count showed 87 per cent polynuclear leukocytes and 13% lymphocytes. Typing at this time revealed a Type I pneumococcus. The blood culture was negative throughout the course of the disease. She ran an remittant type of ^{fever} temperature, rising as high as 105° during the day and as low as 99° in early morning. On Feb. 13, 1932 she delivered a baby girl (premature) with but a few pains (precipitate).^{the} Only medication used up to this time was codiene, grain~~1~~ one-half. Following delivery her symptoms became more marked and she became markedly cyanotic, coughing almost continuously. On February 14, 1932 she was placed in an oxygen tent. She immediately became much more comfortable, less restless and ^{the} cyanosis disappeared, and breathing less rapid and labored. Oxygen 38 to 42 per cent was used. The minute she was taken out of the tent she would become markedly uncomfortable, restless and cyanotic. Breathing would become more rapid and labored.

The only other therapeutic measures used were symptomatic. Morphine was necessary at times to relieve pain. Surgical pituitrin was administered once for distention. At one time ^{the} pulse became rapid, of poor quality and irregular so that digalen 1 c.c. was administered hypodermically. On February 16, 1932, in the afternoon, the patient had her crisis but oxygen was continued

until the following day. The patient's temperature then gradually flattened out and she recovered. She was discharged from the hospital on March 13, 1932 apparently well.

One case is really of no value on which to base conclusions but its marked effect in comforting this patient has led me to believe that it is definitely palliative although probably not curative.

The subcutaneous use of oxygen has been used by a few. Crespigny, (23), treated two cases with apparently marked results. In both cases, the injection was made into the subcutaneous tissue of the axilla and enough introduced to raise an emphysematous area two times the size of the palm. The cyanosis disappeared rapidly, the normal pink color appeared and the patient was markedly less restless and more comfortable.

Diathermy.

Diathermy has been used by some with apparently marked results. Others absolutely are opposed to its use. Probably its therapeutic value lies in the intelligence with which it is administered. Clement, (24), says that pneumonia is one of the most satisfactory conditions to treat with diathermy. The object is to rapidly allay the distressing symptoms as of course it is with all other therapeutic measures. After reviewing the cases which he presents, it seems that possibly diathermy shortened the course of the disease, in that the course was only three to four days for those treated. He used anterior and posterior electrodes, using a block of tin posteriorly and a mesh anteriorly. His dosage usually ranged from 1400 milliamperes on the first day, increasing to 2000 to 2500 milliamperes on the second day for the same length of time, and for each successive day as

long as the symptoms did not change.

Seybold, (25), believes that the earlier the diagnosis of pneumonia is made, the sooner diathermy is applied, the better are the results. He believes diathermy apparently gives the best results, if given early, or during the stage of congestion. The physiological action of diathermy on inflammatory areas being that of hyperemia. Diathermy in his estimation is an absorbent, a dissolvent, a decongestant, an analgesic, a nutrient and a bacteriacidal agent. The local effect therefore being an active hyperemia and softening of the infiltration by the physiological action of heat. Absorption of toxic products takes place through this decongesting process. The capillaries and lymph channels surrounding the congested area are dilated, vasomotor constriction lessened, which has a tendency to increase the flow of blood. This causes the surrounding edema to subside. In pneumonia it is assured that early diathermy has a tendency to keep it in a stage of congestion, which prevents this morbid process from progressing to red and gray hepatization, and in many cases appears or makes one believe that the pneumonia has aborted. At least the temperature subsides and the chest findings are improved. At the first sign of any chest congestion, he therefore advocates the use of diathermy. As to systemic effects of diathermy, there is at times an intense perspiration, which acts as an excellent form of elimination, relieving the cardiovascular and renal systems.

"The influence of diathermy on the clinical picture is at times remarkable. Thoracic pain is lessened, rapid shallow breathing changes into slower deeper breathing, unproductive cough changes into a productive one, the pulse tone improves, meteor-

ism is lessened, that symptomatic relief is obtained is unquestionable."

He uses the high voltage taps on the machine and the usual M.A. is around 2.000 for grownups. This depends upon the patient, type of machine, size of electrodes and the like. The frequency of his machine is 800,000. The duration of the treatment is from twenty to forty minutes. These are given every eight hours or oftener if the case warrents it. Ordinarily they are given twice, or in milder cases once in twenty four hours.

Compressed Air.

Joannides, (26), in a series of experiments with dogs found that the lung expanded when air pressure (intra-bronchial) became 25-30 mm. At between 60-100 mm. mercury there developed interstitial emphysema, pneumothorax, pneumoperitoneum and air embolism. He also found that by severing the heart from connection with the pulmonary vessels and introducing air at a pressure just to distend the alveoli that air escaped ⁿ into the capillaries and that finally all the blood was forced from the capillaries and they became filled with air. When the lungs become immobilized by external compression or drowning with exudate the lung loses its elasticity and little or no air enters or leaves the lung. The result is the heart suffers from overwork and asphyxial charges and the patient collapses because of circulatory decompensation. The pneumonia patient thus needs a supply of oxygen and elimination of waste products as a result of asphyxia.

In experimenting with dogs he finds that when an artificial pneumothorax is developed the blood pressure in the femoral artery shows a gradual diminution in the respiratory waves until finally there is a pulse pressure of zero. At this point the

heart shows a definite brady cardia and soon stops beating. If at any time artificial respiration is instituted the amplitude of the respiratory waves become normal and the animal may be kept alive as long as desired. It is quite necessary that there be some blocking of the outflow of air so as to raise the intrapulmonic pressure to between 20-35 mm. of mercury. He finds that in his experiments where he works under artificial[?] that it is necessary to use oxygen and that it is unnecessary and expensive and that in compressed air there is sufficient oxygen to take care of asphyxia and that by blocking the outflow to raise the intrathoracic pressure the sufficient expansion and contraction reinforces the circulation. Theoretically then by applying this method to pneumonia cases we can visualize how the alveolar walls would be stretched and contracted, how air would find its way into the blood by being of higher pressure in the lung and also how this would do away with anoxemia and reinforce the circulation. He has experimented with dogs with apparently good results, the heart and circulation improved, and that pulmonic and consolidated, dark colored lungs when subjected to increased intrapulmonic air pressure either inside or outside of the body became crepitating and pinkish again. Theoretically this work is fine but in the future maybe some practical applications will be had on which to base some conclusions.

Artificial Pneumothorax

Recently, Coghlan, (27), found that during an investigation into lobar pneumonia he discovered that the induction of artificial pneumothorax had a favourable influence on the progress of the disease.

The induction of the artificial pneumothorax, according to

Coghlan, has the advantage of separating the inflamed pleural surfaces thereby relieving pain and allowing of easy respirations, putting the inflamed lung at rest, and limiting the flow of blood through the pneumonic lung thereby diminishing anoxemia and interfering with the passage of toxins into the general circulation.

He reported six cases on which the method was used. There was one fatality which he attributed to error of judgement in a difficult situation and lack of knowledge of the technique, owing to inexperience; rather than to a defect in the method of treatment.

From these six cases he drew several conclusions. The first was that the induction initiated events very similar to those which normally occur in the disease. The second was that the control of the pneumonic process is at first only temporary, persisting merely as long as air remains in the pleural cavity. Since the absorptive capacity of the pleura in this disease is abnormally high the time taken to absorb the air is a matter of hours only, after which the pneumonic process becomes reestablished at its original level. By adequate refills, he found that the return of the disease can be forestalled, and when the artificial pneumothorax control has been maintained for a sufficient length of time (48 hours appeared to be sufficient) the pathological process is definitely brought to an end, the air can be absorbed without any tendency to relapse, and convalescence proceeds normally.

Quoting Coghlan:- "A striking feature of all the cases was the rapidity of the onset of the artificial crisis; profuse perspiration set in almost as the pneumothorax needle was withdrawn, and cyanosis and dyspnea were relieved in about 15-30 minutes at most, causing corresponding subjective improvement. The fall of temperature was well established in two to three hours, and the

patient lost that appearance of acute distress characteristic of pneumonia."

There are some dangers in the process. The contamination of the pleura in introducing the needle which if ^{it were to} would occur would cause a mixed infection which would be markedly serious. Therefore, at each injection new sites are chosen for the introduction of the needle.

In Coghlan's series, not one developed pleural infection. Cardiac collapse at time of the crisis was thought to be a secondary danger. However, in this instance, where the crisis develops several days sooner the heart is better prepared to meet the crisis and thus probably there is less danger. A definite crisis, however, is to be avoided by only minimal refills at the time perspiration commences and phenacitin, aspirin or Dovers' powders used to help keep up the perspiration so that the fever falls more by lysis and thus, there is less strain placed on the pulmonary circulation and, at the same time, a progressive detoxication will be accomplished.

Coghlan advises the following routine procedure:- "(1) Preliminary medication one hour before induction with morphine gr 1/4 (2) Thorough local anesthesia with novacain down to and including the parietal pleura (3) Very thorough asepsis during induction (4) A preliminary fill of 400-600 c.cm. of air, run in very slowly during the negative phase of the pressure swing cycle, and with the needle clipped off during the high positive phases. (5) A second fill 12 hours later of 300-500 c.cm of air. (6) If the pneumonic process is not completely controlled, a third fill of 100-150 c.cm of air may be given in another 12 or 18 hours. (7) Simultaneous exhibition of a suitable diaphoretic and of Felton's serum in

appropriate cases at the discretion of the operator. (8) Owing to the very profuse perspiration, the comfort of the patient is much enhanced by warm sponging p.r.n. and nursing between blankets. (9) In cases where it is deemed inadvisable to provoke defervescence by crisis, and gradual fall by lysis is aimed at, three fills of 100-150 c. cm. at intervals of six hours might be given and further treatment judged by results."

Serum Therapy

Since the beginning of the twentieth century, it has been proven that certain elements such as opsonins, agglutins, precipitins etc. act as antibactericidal agents. Thus the pneumococcus has been one of those organisms on which much work has been done to develop these elements. According to Howard, (1), the primary work in this direction was done in Germany. However Cole in America took up the suggestion and found that he was successful in immunizing horses against types I and II pneumococci but not type III or IV. The method of immunizing the horse was by daily injections of dead pneumococci of a specific type for at least seven injections. This set up an immunization in the horse, the attempt being made to get the serum of such strength that 0.2 c.c. will protect ^{2,} mich against at least 0.1c.c. of a culture which is of such virulence that 0.000001 c.c. of an 18 hour broth culture will kill a mouse of 20 gm. weight within forty eight hours. The horse is then bled and the serum is separated from the clot and placed in bottles.

In using the serum, one must keep in mind the fact that the earlier it is given the better are its' therapeutic effect. Many think that after the third day of the disease that it is of little value. Thus, a search has been made for a quicker way of typing

the patient than the mouse injection method which requires at least 24 hours for good results. Therefore, it seems that there probably are only a very few cases in which the serum can be used to advantage, owing to the fact that many cases are not seen before at least the second day and also the delay due to typing. If the serum is used, Cole believes, in first seeing if the patient is sensitive to the serum by injection^{ing} into the conjunctival sac of a few drops of the serum or the administration^{ing} of a few drops intradermally, and watch for a reaction as evidenced by hyperemia. The patient should also be questioned in regard to asthma, hay fever and ^Yusticania^Y. If the patient is sensitive 5 c.c. of the serum may be injected slowly subcutaneously to render desensitization, (waiting^{after} one half hour ~~before administration of the dosage.~~) The patient is then given 100 c.c. intravenously by gravity method every 48 hours until crisis occurs. In case of an anaphylactic shock adrenalin should always be at hand for injection.

In reviewing the literature I find the results with the type I antipneumococcus serum striking in that nearly all authors write that it lowers the mortality anywhere from 5 to 30 per cent. The results with type II are not so striking. The usefulness of this serum seems to be rather limited to hospital practice because of its bulk, its technique of administration and the protein reactions.

Brown treated 22 cases, using antipneumococcus serum according to the above described technique, 14 of type I in which he had two deaths and 8 of type II in which he had 1 death. This is only a small series of cases but the results are very similar to findings in the larger series. The noted effects were that, symptomatically, the change is very striking, from a marked distressed condition to a much more comfortable condition. The period of

toxicity is greatly reduced. Natural sleep returns more quickly as does appetite. Convalescence is more rapid. The temperature usually drops rather abruptly following the use of serum.

Cruikshank, (29), finds that the quickest method of typing is to inject an initial dose of polyvalent I and II antipneumococcus serum. In six to eight hours a little blood is taken from the ear and tested for presence of agglutinins. If agglutinins I are found the type is said to be II, and visa versa, since the agglutinins are neutralized by the infecting organisms.

According to Howard, (1), Huntoon, in 1921 developed a polyvalent serum containing antibodies of types I, II and III. According to Cecil, (6), this serum is a water soluble extract of immune bodies taken from astipneumococcus horse serum. It contains the antibodies for types I, II, and III but not in concentrated form. Its disadvantages are that it does not have adequate potency and tends to produce sharp chills when given intravenously. It has been practically discarded.

The most recent effort to refine and concentrate antipneumococcus serum has been done by Loyd Felton. The serum, according to Cruikshank, (29), is made by injecting a horse with killed virulent organisms and then bled. The serum is allowed to separate off and sodium phosphate is added and incubated at 37°C. until a precipitate forms. The precipitate is dialyzed in water for 5-7 days and the contents of the sac is raised to a PH of 4.6 where another precipitate forms and is removed. The supernatant fluid is diluted 4-5 times. There is an elimination of the albumin fraction which is so responsible for anaphylactic reactions. This sera is rich in opsonins and agglutinins and is antibactericidal not antitoxic and acts directly on organisms making them sus-

ceptable to phagocytosis. This serum contains, on an average, 2000 units against type I and 1000-2000 units against type II.

Fleming, (30), says the method of administration may be either intramuscular, subcutaneous or intravenous. The intravenous method is more commonly employed since the antibodies of the horse serum are precipitated out and are thus less likely to produce shock. The serum is heated to 100^oF. before administration. Before administration, a small amount is instilled in the left conjunctival sac and if the slightest redness occurs the serum is contraindicated until desensitization of the patient is done. If the patient gives a history of asthma, hay fever, urticaria or ^{has} had previous serum treatments it is absolutely contraindicated. The serum is injected into the antecubital vein taking at least 10 minutes for the first c.c. and five minutes for the rest of the dose. The doctor should keep his finger on the pulse during the entire procedure, as any change in the quality or rate of the pulse indicates a reaction. The dosage given is 10 c.c. which can be repeated every 8 hours as evidenced by the condition of the patient. Repeating of the dose is indicated if the patient has a temperature beyond 102^oF. or signs of toxemia as evidenced by delirium, exhaustion, incontinence etc.

Fleming's, (30), view, with which serum is used, is to ward off a septicemia and maintain a sterile blood, not to overcome the primary focus in the lung as this will usually take care of itself.

Cowan and Harrington, (31), treated 57 cases of lobar pneumonia with Felton's serum with a mortality of 10.3 per cent in contrast to their old series of 856 cases treated without serum with a mortality of 18.4 per cent. Quoting them "Felton's serum

is effective with types I and II infections alone. It has no effect on other infections. It seems clear that lobar pneumonia as recognized clinically, is due to a pneumococcal infection, and that more than half of the cases are due to infection by types I or II. The occurrence^{ve} of pneumonia in an adult is, we think, an indication to exhibit Felton's serum at once, and to continue its administration until the patient is better, or bacteriological investigation shows that type I or II is not the causal organism in the particular case."

Finland and Sutliff, (32), recommend 100,000 units given within the first 24 hours. They report treatment of 59 cases at the Boston City Hospital. Twenty-seven cases were treated with sera and given large doses early in the disease. Indications of improvement were duration of disease, course of bacteremia and presence or absence of pulmonary extensions. Results showed that marked improvement resulted where serum was given early in the disease and in high dosage whereas if given in the first 24-30 hours seven of the treated cases extended over a period of only three days as marked by the absence of temperature. However, if given late in the disease less value was attached to its usefulness.

They found the sera to be of marked value both in preventing and eliminating bacteremia. All cases having a bacteremia and treated by sera showed no positive blood culture anytime after administration of sera, and no case having a negative blood culture developed a positive.

Cecil, (6), remarks that it is interesting to note that monkeys can be given classical lobar pneumonia by intra-tracheal injection of type I pneumococcus. As soon as the classical symptoms of pneumonia present themselves they administer Felton's

serum and find that almost immediately the temperature begins to fall and symptoms begin to disappear whereas the control group of monkeys die.

About 500 patients are received into the medical wards of the Bellvue hospital each year and they give each patient a number, the odd numbers receive the serum and the even ones do not. The patients are asked if they ever had asthma, hay fever, or urticaria and a skin test or ophthalmic test is done. If all is negative, 5 c.c. of Felton's serum are given at once, intravenously, watching the patient closely. If there are no symptoms of anaphylaxis, the patient is given 50 to 75 c.c. on the first day. The subsequent day the dosage is governed by the reaction of the patient. Usually the temperature and other symptoms have subsided somewhat and 15 to 20 c.c. are given on the second day. Out of 44 cases receiving serum 10 to 12% showed serum sickness which came on 1 to 2 weeks after injection. In 153 treated cases of type I pneumonia, there was a mortality of 20.6 per cent. In type II, the results were not so good, 41.5 per cent mortality for treated and 54.5 per cent in the untreated series. In type III, 40 per cent for treated and 28.6 per cent for untreated. In type IV, serum appeared to be of benefit in that there was a mortality of 28.2 per cent for treated cases whereas there was a mortality of 38.3 per cent for untreated cases. The death rate, for 441 treated cases, was 30 per cent whereas for 444 untreated there was 39.2 per cent. Cecil, (6) believes that individuals, under 40 years of age, should receive Felton's serum before taking time to receive laboratory data as it takes too long. Two thirds of these patients will be benefited because types I and II occur about that often under that age. All patients over 40 years

should have their sputum typed before any serum is given as about two thirds of these cases are of type III or IV, and since there is no sera for these groups Felton's is useless.

Baldwin,(33), firmly believes that there are obvious advantages of the concentrate prepared according to Felton over whole serum. The factor of concentration, expressed in terms of units, is very helpful in fixing the dose and affords greater facility in administration, owing to its smaller volume. The dosage varying from 5 to 30 c.c. per dose with the concentrate as opposed to 50 to 200 c.c. when whole serum is used. The disadvantages, inherent in any modification of whole serum consisting principally in thermal or chill reactions, are becoming less pronounced. Less than 10 per cent of all injections are followed by chill reactions. On the other hand, serum sickness is largely eliminated, less than 25% of the cases having this complication, and when it does occur it is mild, causing only brief discomfort incomparable in severity with that produced by the use of the whole serum.

Conclusions.

1. Proper management of the pneumonia case, and possible vaccination in crowded districts, tends to restrict the incidence of pneumonia.
2. Proper management, especially in the form of nursing, is a valuable asset to the pneumonia patient.
3. The benefits which are derived from morphine, in the relief from pain, reduction of metabolism, and sleep, far outweigh any ill effects that may be derived from it. Therefore, it should be used in pneumonia for these purposes when other measures fail.
4. Turpentine stupes or enema are valuable to remove distention but if these measures fail the use of surgical pituitrin is indicated.
5. In severe pneumonia cases, digitalis probably should be administered in small dosage so that if its action is desired later in the disease less time will be required to obtain its physiological action. In less severe cases, it should not be used unless it becomes indicated later in the disease.
6. Bleeding, although practiced by the ancients, is probably still valuable in relieving distention of the right side of the heart late in the course of the disease.
7. Adrenalin and atropin are probably the best cardiac stimulants in time of collapse.
8. Glucose is valuable in that it is a simple means of providing the patient with calories. By mouth is as valuable as by vein. If the patient cannot take it by mouth then it should be given intravenously.
9. There are no specific drugs used in the treatment of pneumonia

but a few are valuable if properly employed.

10. Oxygen is of value as a paliative measure in relieving cyanosis and restlessness. The oxygen tent method, with a saturation of at least 40%, is probably the best method of administration.
11. Diathermy has proved valuable in a few hands.
12. Theoretically, compressed air is of value.
13. Production of artificial pneumothorax seems to be a step forward in the treatment of pneumonia. However, it is only in its infancy and further tests will prove its efficiency.
14. Serum is highly useful in the treatment of types I and II infections but of no value in types III and IV. Best results are obtained when used early in the disease and in high dosage. It prevents and eliminates bacteremia. There are many advantages of Felton's serum over whole serum. It is concentrated and thus requires less amount per dose. There is an elimination of the albumin fraction which is so responsible for anaphylactic reactions.

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