UNIVERSITY OF MINNESOTA

Pneumococcic Pneumonia

Volume VI | Thursday, April 11, 1935 | Number 24

UNIVERSITY OF MINNESOTA HOSPITALS
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INDEX

COURTESY OF CITIZENS AID SOCIETY

THE MAX VANDER HORCK LECTURESHIP IN DERMATOLOGY

Sponsored by the Minnesota Dermatological Society

Will Be Given By

PROFESSOR FRANZ BLUMENTHAL

Berlin and University of Michigan

SUBJECT

"PARADOXICAL INFLUENCE OF LIGHT

IN SKIN CANCER"

Thursday, April 18, 12:30 p.m.

Medical Sciences Amphitheater

I.

SPECIAL NOTICE

Professor Blumenthal was invited for our Staff Meeting. It was thought advisable to hold this meeting in a larger and more accessible place. The procedure next week will be as follows:

Luncheon: 11:45 - 12:15, in the usual way. We will then go to the Medical Sciences Amphitheater for the lecture. The Bulletin will be issued the following week.

It is earnestly hoped that all will find it possible to attend.

II. ABSTRACT

PNEUMCOCOCCIC PNEUMONIA (LOBAR)

R. W. Koucky

References

1. Reimann, H. A., Tillet, W. C., and Rigler, L. G.
Acute Lobar Pneumonia.
Cyclopedia of Med. 1028-1114.

2. Reimann, H. A.
Personal Comments.

Terminology

Pneumonias are generally subdivided into two groups: lobar pneumonia and broncho-pneumonia. It is quite obvious that both of these terms are unsatisfactory because they denote neither the etiological factors nor the anatomical distribution. Lobar pneumonia frequently is not lobar in distribution. "Broncho-pneumonia" indicates origin from the bronchi and by distinction, "lobar" pneumonia suggests a different mode of origin. Since this is unknown, such a distinction should not be made. In all varieties of pneumonias, inclusive, a wide range of etiological factors are present. In "lobar" pneumonia, the bacterial agents involved may be pneumococci, streptococci, staphylococci, Friedlander's bacilli, etc. Even within the pneumococcus group, a division according to the types of pneumococci is indicated because of the difference in the course, outcome and complications peculiar to each type. It is suggested, therefore, that the terms pneumococcic pneumonia type I, II, III, etc., streptococcic pneumonia, staphylococcic pneumonia are preferable.

Etiology

Pneumococci: The general characteristics of pneumococci are well-known and need no special description. However, there are some important features which can be reviewed at this time.

Pneumococci have a very delicate growth requirement when first isolated from the body. This is of importance in interpreting the result of cultures. On the usual media, the cultures may be sterile and when there is a mixed infection present the pneumococci may be overgrown. Mouse inoculation is the most favorable method of isolating this organism but it should again be remembered that by means of this method pneumococci alone are recovered and other contaminating organisms may be lost.

The type specific pneumococci all possess a capsule. The reactions of this capsular substance are probably the most interesting features of the organism. Chemically, it is a polysaccharide which varies slightly in its composition according to the specific type of the organism. The type specificity, i.e. Type I, II, III, depends upon this chemical composition of the capsule. It also appears that virulence of the pneumococcus depends upon the presence of a capsule.

This capsule yields a soluble substance which appears in the serum and the urine of patients with pneumonia. This is the substance which is combined or neutralized by the antisera and, therefore, it appears to be the nature of toxin (antigen). It is hoped that future experimental work will devise a method by means of which the amount of this specific soluble substance within the blood serum may be measured so that the proper amount of neutralizing antiserum can be administered.

Recent experimental work has produced an enzyme recovered from cultures of certain bacteria which specifically neutralizes the soluble substance produced by the pneumococcus, Type III. This bacterial enzyme is as yet not available for therapeutic purposes.

Bacterial body: The bodies of the bacteria, exclusive of the capsular substance, are a protein material which appears to be alike (antigenetically) in all the various types of pneumococci.

Antibodies prepared against this protein substance act equally well against the protein of pneumococcus, Type I, II, III, etc.

A third substance has been recovered from cultures of pneumococci which appears to be different from both of the specific soluble substance found in the capsule and from the protein material recovered from the bacterial bodies. When injected, intradermally, it produces a red reaction about the site of injection. This material acts as an antigen and an antiserum has been prepared. Its importance and action has not been determined.

Hetrophile antigen: The investigative work on hetrophile antigens has shown that pneumococci also possess this property. Pneumococci when injected into an animal produce an antibody which causes agglutination of sheep cells (hence, the term "hetrophile antigen"). Its significance likewise has not been shown.

Pneumococcus antisera: It is apparent from the previous that several types of antibodies may be produced experimentally. Only one of this group has been proven to be of any clinical value, i.e. the type specific capsular antibody. Within the past few years through the use of these type specific antibodies, the pneumococci have been further subdivided. Previously, the division has been into Type I, II, III and IV. More recently, the Group IV has been subdivided into 29 individual subgroups. While diagnostic sera used for identification of the types are available, sera which may be used for therapeutic purposes have been developed only for certain types, i.e. for Type I, II, and VII.

Recently, there appeared on the market so-called "antipneumococcus sera" which contain all the possible antibodies which can be produced. This includes the type specific capsular antibodies, the protein antibodies, hetrophile antibodies (described above) and the antibody against the so-called "toxic" substance recovered in the filtrates of cultures. This serum is being given clinical application and its value as yet is to be determined.

Other Etiological Factors

It is difficult to estimate concretely the importance of various predisposing causes. Many of these are not constant. Other features appear to be more conspicuous but are difficult to interpret. Individual predisposition to the disease or local susceptibility (in the lungs) are indefinite factors. General lowered resistance increasing the susceptibility to pneumonia is folk lore. Chilling of the body, exhaustion, dissipation and similar causes are often strikingly associated with the onset of lobar pneumonia. The mechanism however is not known. Age undoubtedly plays a part since the disease is definitely a disease of middle life.

Decade	No. of Cases
1	600 - 700
2	400 - 500
3	1300 -1400
4	1400 -1500
5	1200 -1300
6	700 - 800
Over 60	500 - 600

(Figures taken from a curve; exact figures not stated.)

Certain races show difference in resistance to the disease. In negroes, the mortality is about three times that in whites. The Chinese are said to have a much lower rate although accurate statistics are difficult to obtain. Males are involved more frequently than females but this may be due to differences in the exposure to cold, exhaustion, etc. There is a very definite correlation between the incidence of pneumonia and the season. In one study extending over a 10-year period of time, there was a constant peak of incidence occurring in the mid-winter months.

Epidemiology

The incidence of pneumonia is difficult to determine accurately from the statistics because the term "pneumonia" is used indiscriminately. In the records of the Surgeon General, there were 1.01 deaths per thousand inhabitants. In the statistics gathered from 52 life insurance companies, there was a .8 mortality per thousand deaths. During the World War, there were 58,119 deaths from disease of which 11,329 were classified as lobar pneumonia. This is an incidence of 19.5% or 195 per thousand deaths.

The contagiousness of pneumococcic pneumonia was recognized as early as 1497. In recent years, it has been possible through the typing of pneumococci to distinguish the normal inhabitants of the throat (Group IV) from the pneumococci responsible for lobar pneumonia. There is no longer any doubt but what the type specific I, II and III pneumococcic pneumonia are transmitted from patient to patient. When conditions of crowding, unsatisfactory isolation and lowered resistance arise, pneumonia frequently occurs in epidemic form. This is best illustrated in the army camps during the World War, in the Panama Canal construction camps and in the African Rand mining camps.

Pathology

The classical gross and microscopic picture of lobar pneumonia needs no review. In recent years, studies of the initial lesion have been made but these have not given conclusive results. There are various theories as to the initial focus and its spread but many of these are contradictory. It has been commonly stated that the right side is most frequently involved but recent statistics show that the left is equally or slightly more frequently involved.

Symptoms and Course

The exact incubation period is difficult to determine. It apparently may be very short as indicated in the following table:

Incubation Time of 20 Cases of Pneumonia

No. of Cases	Incubation Time
3	1 hour
3	2 hours
3	3 "
5	4 "
3	5 "
1	6 "
1	12 "
1	24 "

The actual onset of the disease is frequently preceded by upper respiratory infection, bronchitis, malaise, headache and body pain. In Cole's cases, this was present in 40%; Adams' cases, 26%; Cecil's, 48%.

The onset is sudden in 75% of the cases. Usually, there is a chill or less often sensation of chilliness. As soon as the chill subsides, the temperature rises often as high as 104 and the patient has a sensation of fever. The face is flushed and anxious, the tongue is dry, the pulse and respirations become elevated. From 8 to 24 hours, there develop pleuritic pains, cough and expectoration of rusty sputum.

The usual or average case of pneumococcic pneumonia has a fairly typical and constant course extending from 4 to 10 days. Some of the variable factors which appear to modify this typical course are extreme dyspnea and cyanosis, headache, jaundice, distention, delirium, hiccoughs, etc. Sudden marked changes are well known. A moribund patient may suddenly become improved and likewise a patient who was considered to have a good outlook suddenly becomes much worse. The unfavorable signs consist of exhaustion, high pulse rate, cardiac irregularity and marked cyanosis. Death is usually due to exhaustion, cardiac failure and edema of the lungs.

Course with Regard to Pneumococcus Type

Type I: The infection with this organism presents the most uniform and typical course. The outstanding characteristic is the incidence in young adults in good health, the generally better outcome and the high incidence of complications (about 12%, nearly double).

Type II: The pneumonia in this case is probably the most severe of any of the group. Blood cultures are frequently positive and the mortality with a positive blood culture is about 90%.

Type III: The characteristic feature is the gradual onset frequently without a chill, usually with a history of a preceding respiratory infection. The patients involved generally are much older than in the previous groups and the disease often is secondary to some other systemic illness. The sputum is atypical. The mortality of this type of pneumonia is said to be very high. The older literature gives it as 65%. Analysis of this, however, shows that the disease is quite common in elderly individuals and is often secondary to other diseases which probably account for the increased mortality. In previously healthy young adults, the mortality of Type III pneumococcus is only about 8%.

Group IV: This type of infection is rarely true lobar pneumonia. Most frequently the pneumonia is a mixed infection with streptococci, staphylococci and other organisms and the anatomical lobar distribution is frequently due to a confluence of a patchy pneumonia.

Clinico-pathological Features of Symptoms

Fever is ushered by chills in 40 to 70% of the cases. When the chills subside, the temperature is elevated (as high as 104) and reaches its maximum in one to two days. For a period of 4 to 6 days, the temperature remains fairly constant and may be as high as 106. The temperature becomes more irregular as crisis is approached. The duration of the pneumonia, as indicated by the fever, is given in the following table:

Duration of Disease in Untreated Patients Who Recovered (Cecil, Baldwin and Larsen).

Type of Pneumococcus	Cases	Average No. of Days
I	264	8.8
II	117	8.6
III	85	9.1
IV	226	8.7

Crisis: The sudden drop of temperature in a period of 12 to 36 hours is a phenomena which is unusual in fever and is characteristically found only in pneumonia and typhus fever. The mechanism producing crises is unknown. Various theories have been presented such as neutralization of toxin, accumulation of antibodies, sudden inhibition of the growth or destruction of the pneumococcic and allergic changes but no definite conclusions can be drawn. The frequency of crisis is indicated in the following table:

Incidence of Crisis and Lysis in Untreated Patients
(Cecil, Baldwin, Larsen)

Type of Pneumococcus	Total Cases	Crisis	Lysis	% With Crisis
I	285	146	112	56.6
II	122	61	61	50.0
III	89	35	54	39.3
IV	248	113	135	45.5
	744	355	362	Average, 49.6

The day of crisis occurs as follows:

Duration of Fever in 873 Cases in Which Crisis Occurred (Aufrecht)

Day	No. of Cases		
1	1		
2	2		
3	61		
4	53		
5	123		
6	116		
7	155	68.2%	92.3%
8	95		
9	127		
10	50		
11	50		
12	9		
13	16		
14	6		
15	1		
16	3		
17	1		
18	2		
20	1		
22	1		

Pain: The thoracic pain is said to be due to irritation of the pleura either by direct infection, stretching or lymphangitis. The transmission of the pain to the abdominal area is not uncommon. In 145 children with the diagnosis of appendicitis, 25 were found to be suffering from lobar pneumonia. In 658 cases of lobar pneumonia, 7.7% had abdominal pain.

Dyspnea and Cyanosis: It is generally assumed that the respiratory changes are dependent upon the amount of consolidation in the lungs. This is undoubtedly true to a certain extent but many other factors are also present. The involvement of the pleura and inflammatory reaction about the nerve ending may produce a reflex nervous elevation of respiratory rate. Increased carbon dioxide concentration within the blood may be a factor in some cases but is certainly not acting alone. The degree of anoxemia undoubtedly is a factor. In normal individuals in case of mountain sickness, 85% (of normal) oxygen saturation produces vertigo, restlessness, palpitation of the heart, dyspnea and cyanosis. It has been shown that 90% saturation will induce cyanosis. In cases of pneumonia, the degree of anoxemia many times is much more severe (as low as 65% saturation).

Heart: The usual pulse rate ranges between 90 and 130. About 95% of the patients show sinus arrhythmia. About 5 to 8% show auricular fibrillation. Electrocardiograms have been variously interpreted and it is questionable whether there is any significant change. The blood pressure quite frequently falls 15 to 20 mm. It is commonly said that if the blood pressure expressed in millimeters of mercury is higher than the pulse expressed in beats per minute, the prognosis is good (Gibson's rule). A great many factors may enter the picture to modify this rule. Death in lobar pneumonia frequently appears to be due to circulatory collapse. Three factors are suggested: (1) Through experimental and clinical observation, there is evidence to indicate that the consolidated lung offers resistance to the circulation of blood. (2) Autopsy studies have shown degeneration of heart muscle (toxemia?, anoxemia?): 42% of the cases in one series. (3) Anoxemia may be an important factor. The lowered oxygen supply undoubtedly interferes with the heart action. A previously normal heart may overcome this but one damaged by previous disease may succumb.

Metabolism: Basal metabolic rate during pneumonia is increased from 36 to 40%.

Chemistry: The body metabolism as indicated by the chemistry shows certain definite changes which however are very poorly understood. There is a marked increase in the nitrogen output in the urine following the crisis. During the period of the fever, there is increased output of uric acid, creatine and creatinine. Following the crisis, there is a diminution in the output. Blood cholesterol is decreased and hypocholesteremia may be present during convalescence. In children particularly, a high organic acid content is present in the urine during convalescence. Diminution in chloride output has been observed for a long time. A lowered output

in the urine is frequent in any fever but in pneumonia the chlorides are reduced to zero. The blood chlorides are low. Examination of the various tissues including consolidated lung failed to indicate any increased storage of chloride. The disturbance in this chloride metabolism is not understood. Chloride administration as a form of therapy is not advised since edema has resulted in some cases. Water retention apparently takes place during the acute illness since increase in weight has been observed and particularly since there is a very definite increase in water output after the crisis.

Jaundice: Incidence has been recorded as follows:

Author	%
Chatard	11.5
Norris	1.6 (22,544 cases)
Schiff	2.5

The cause of the jaundice is indefinite. It has been suggested that congestion of the liver, hepatitis on the basis of fever, anoxemia of liver, hemolysis of the red blood cells in the exudate within the lung, and hemolysis of the circulating blood cells may be the cause.

Leucocytosis: The average leucocytosis in pneumonia is about 25,000. Approximately 90% of cases have a leucocytosis over 10,000. Low count, i.e. below 10,000, have a much higher mortality (45%). The significance of this however is questionable in the light of certain experimental work with benzolized animals. Pneumonia in these animals which have granulopenia apparently has the same course and same mortality as in untreated animals.

Septicemia: It is usually said that the incidence of positive blood cultures is about 25%. Cole in his series had an incidence of 28%; Cecil, 27%. In another series in which cultures were taken more frequently, the incidence was 34%. The variation in incidence of positive blood cultures according to the pneumococcus type is given in the following table:

Results of Blood Cultures in 433 Cases of Pneumococcus Pneumonia

Type of Pneumococcus	No. Cultured	No. Positive	%
I	164	44	26.8
II	97	45	46.4
III	47	14	29.8
IV	125	23	18.4
	433	126	Average, 29

Physical Findings

The physical findings in lobar pneumonia do not require any special discussion.

Complications

The authors describe the type, incidence, physical findings, differential diagnosis, treatment of complications. In order to limit the present discussion, this phase of the problem is omitted.

Diagnosis

"In a patient, previously well, who is suddenly taken with a chill and develops high fever, cough, pain in the chest, rusty sputum, together with signs of consolidation in the lung, there is little doubt as to the diagnosis of lobar pneumonia." However, in some cases, the characteristic history may be obtained with indefinite or absent findings on physical examination. In such cases, emphasis must be placed upon laboratory procedures (see x-ray diagnoses below).

Laboratory Diagnosis

Bacteriological examination is of extreme importance in diagnosis. The isolation of the organisms should be done from both the sputum and the blood when possible. Sputum should be collected immediately for inoculation into a mouse and the diagnosis and type of

organism may be obtained within 6 to 10 hours. In some cases, the organisms isolated by this method will belong to the Group IV group. In such cases, suspicion should be aroused that the type specific pneumococci were not obtained and the sputum examination should be repeated.

Blood cultures when positive frequently show the presence of the organisms as early as 6 hours. The value in prognosis and in treatment will be discussed later. In case Group IV, organisms were recovered from the sputum, the presence of other type specific pneumococci in the blood culture is of extreme importance in establishing a correct diagnosis. This error of recovering Group IV pneumococci in cases actually due to type specific pneumococci apparently is present in about 15% of Group IV typings.

X-ray Diagnosis

The relation of the opacities of the lung, mediastinum and liver are such that they offer almost ideal conditions for accurate analysis by means of the x-ray. Many times the initial x-ray with frequent repeats during the course of the illness offers a more accurate picture than the autopsy.

The onset of x-ray signs may be as early as 12 or 18 hours after the initial symptom, and usually within 24 hours they are diagnostic.

The initial lesion: There are two theories as to the location and significance of the initial lesions in pneumonia. One group believes that the first findings are at the periphery of the lung and the other group believes that the initial lesions begin at the hilus and extend peripherally. It has been shown (Ude) that many of these central shadows (in A-P roentgenograms) are really peripheral when examined from different directions. It is the author's impression (Rigler) that most pneumonias begin as a peripheral consolidation. In the usual antero-posterior roentgenograms, there are 3 types of early lesions which are visible. The first is a veil-like cloudiness over the entire lobe which in 12 to 24 hours becomes a characteristic homogenous density. The second is the peripheral wedge with its base at the pleural surface which either remains atationary or slowly spreads. The third is the central rounded shadow near the hilus with an irregular border which gradually extends peripherally to involve the entire lobe.

Accurate localization of the pneumonic process as to lobes involved depends upon an accurate interpretation of the roentgenogram and upon several roentgenograms taken in different directions.

Crisis: At the time of crisis, no definite change is visible in the degree of consolidation. Within 24 hours after crisis, the shadow begins to break up and gradually diminishes in intensity. For a short period of time during convalescence, there are feathery, irregular shadows throughout the lobe.

Complications: Frequently these can be made out very early in the course of the illness. Thickening of the pleura, adhesions of the pleura and empyema (diffuse, interlobar and encapsulated types) can be seen.

Prognosis

The mortality stated in the literature is about 25%. Kelly in 6500 cases had a mortality of 36%; Cecil in 2629 cases, 32%. The mortality of the different types may be seen in the following table:

Type of Pneumococcus	No. of Cases	%
I	352	20.7
II	221	42.0
III	161	41.6
IV	373	29.2

The comparative death rate in cases with negative and positive blood cultures is indicated in the following:

Type of Pneumococcus	Death Rate in Cases with Negative Blood Cultures		Death Rate in Cases with Positive Blood Cultures	
	No. of Cases	% Fatal	No. of Cases	% Fatal
I	92	15.2	33	72.7
II	47	16.2	31	90.3
III	26	41.5	10	80.0
IV	75	16.0	15	93.3
	240	Average, 18.7	89	Average, 83.1

When the pneumonia is complicated or occurs with other systemic disease, the death rate is shown in the following table:

Type of Pneumococcus	Cases with Systemic Disease		Cases Without Systemic Disease	
	Cases	% Fatal	Cases	% Fatal
I	61	37.7	237	14.3
II	67	56.7	136	36.7
III	83	66.3	48	8.5
IV	116	33.6	254	27.5
	327	Average, 46.4	675	Average, 23.4

The outcome according to the involvement is as follows:

	Cases	%
One lobe	1158	20.9
Two lobes	555	36.3
Three lobes	154	40.8
Four lobes	26	65.5

The mortality rises very high in the presence of complications as indicated in the following table:

	%
Cases complicated by empyema	38
Cases complicated by meningitis	99
Cases complicated by arthritis	65
Cases complicated by endocarditis	99
Cases complicated by pericarditis	88

Prophylaxis

It has been known for ages that avoiding exposure to wet and cold and a hot bath, hot food or hot drink with rest following exposure are excellent prophylactic measures. The author (Reimann) emphasizes very strongly that pneumonia is an acute infectious disease and should be treated like other communicable diseases. Isolation technique should be carried out completely. Immunization against pneumonia is in an experimental state and no conclusions can be drawn.

Treatment

The author (Tillet) divides the treatment of pneumonia into 5 divisions: (1) therapeutic procedures, maintaining the general condition; (2) procedures directly toward special conditions; (3) type specific serum treatment; (4) special methods; (5) treatment of complications. In this abstract, only the type specific treatment and the special methods will be reviewed.

Type Specific Serum Treatment: Sufficient experimental and clinical evidence has now been accumulated to indicate clearly that this type of treatment has definitely lowered the mortality in certain types of pneumococcic pneumonias. From this experience, it would appear that the patient with a positive blood culture and those who are treated within the first three days derive the greatest benefit.

Skin Test: Since each pneumonia patient becomes a prospective candidate for serum treatment, the sensitivity to horse serum should be determined on the first visit. In the interval while the diagnosis as to the specific type of pneumococci is being determined, desensitization can be carried out if the patient has a positive skin test. Valuable time may be saved by this procedure.

Methods: Serum is available now in two forms: either the unconcentrated or the concentrated solution. The unconcentrated type is no longer in general use.

The concentrated solution is marketed in terms of "units." It has been found that the antibodies adhere or are absorbed on the surface of the globulin particles in the serum. Therefore, it has been possible to concentrate the antibody by salting out the globulin. This is known as the Felton concentrated serum. It has been standardized in terms of units. One unit is the amount of antibody which will protect a mouse against 1,000,000 times the lethal dose of pneumococci. The dose which is advocated is 10,000 units each 8 to 12 hours until the temperature remains below 101. The author feels that this amount is too small and either the dose should be increased or the time interval should be shortened.

Results: The results of serum treatment are as follows: Cole in 371 cases of Type I pneumococcus pneumonia had a mortality of 10%. Cecil and Sutliff in Type I pneumococcus pneumonia reduced the mortality from 33% to 21% and in Type II pneumonia from 54.5% to 41.5%. Park, Bullova and Rosenbluth give the following results: (approximate figures are given. These are taken from a graph in which exact figures are not stated.)

	Positive Blood Culture Mortality %	Negative Blood Culture Mortality %
Type I without serum	70	18
Type I with serum	35	10
Type II without serum	82	18
Type II with serum	50	14

Special Methods: The author mentions three special methods which have been used in the treatment of pneumonia: optochin (ethylhydrocuprein), diathermy and carbon dioxide inhalation. The results with diathermy and carbon dioxide inhalations have not proven very convincing. The experimental results with the use of optochin have not been encouraging although the drug has a marked bacteriocidal action on pneumococci. However, in clinical practice, the results have been disappointing. Possibly a much larger amount of the drug might give results but it would be toxic in this quantity.

Impressions

The impressions obtained from the work of these authors may be summarized as follows:

1. Pneumonia is a problem being intensively studied over the entire world.

2. The academic bacteriological studies of pneumococci (identification, biology,

antibody formation) are being rapidly absorbed into clinical practice.

3. The outstanding features are the intensive study of the organisms, the clinico-pathological analysis of the symptoms, the definite reduction in mortality through application of serum treatment and finally, the hope that is held out that further improvements in treatment may be possible.

III. MOVIES

Title: Around the Acropolis

Released by: The Fox Motion Picture Corporation.

IV. A NOTICE TO THE STAFF

Your attention is called to the order of the Police Department, published in the Official Minnesota Daily Bulletin. We have been informed by the Police Department that parking ordinances will be enforced on all grounds adjacent to the University Hospitals at once. Parking signs and yellow curbs must be observed. If you are not in possession of a staff parking permit you may obtain one by applying at the office of Mr. Amberg, Assistant Director.

Halbert L. Dunn, M.D.
Director.