Bulletin of

Staff Meeting

University of Minnesota Hospitals

Minneapolis

Vol. V
No. 19
4-12-34

Fat Embolism

VOL. V THURSDAY, APRIL 12, 1934 NO. 19

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COURTESY OF CITIZENS AID SOCIETY

I. ABSTRACT

FAT EMBOLISM

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Historical

The history of fat embolism is approximately 100 years old. Magendie (1821-1836) injected fat intravenously into experimental animals and his descriptions of the pathology and symptoms were excellent. Warthin lists 6 investigators up to 1860. In this year Muller observed fat in the retinae of a patient with nephritis and Cohn found fat emboli in the brain of another patient. In 1862, Zenker described the first case of pulmonary fat embolism. Immediately thereafter numerous articles appeared. Bergman (1873) was the first to make a diagnosis of fat embolism during life. Riedel in 1879 observed fat droplets in the urine of patients with fat embolism. In 1880, Scriba collected 177 cases from the literature and added 34 of his own. This was the first extensive critical review of the subject. From this time on many articles appeared. Among these, two frequently referred to are those of Payr (1899) and Grondahl (1911). In the American literature during this period, there were only a few publications on fat embolism. Warthin mentions only 15 up to 1913. This author published his monograph in 1913 and it remains as the authoritative work in the English speaking countries to date. Killian in 1931 presented another very extensive review of the entire subject. This author out of about 200 papers found only 33 written in any other than the German language. These last 2 articles, totalling 145 pages, cover all the phases of the problem.

There can be no longer any doubt as to the possibility of fat emboli producing death. The older discussions as to the origin and transportation of the fat seem to be entirely out of date. Warthin stated that the condition is not rare and is probably the most frequent cause of death after fractures of the long bones in the absence of infection.

Incidence

There are wide differences in the reported frequency of fat embolism. Warthin was able to collect about 350 cases from the literature. 86 of these were reported in the first 17 years after the stimulus of Zenker's description. He himself in a small autopsy series of 560 examinations found 12 fatal cases. Killian had 112 original cases. This illustrates that the incidence depends upon the examiner.

Another factor causing the great differences in incidence is the type of material, i.e., the percentage of severe accidents. And finally, the incidence found at postmortem examination is much greater than the incidence clinically.

The following tables illustrate these points:

Author (from Killian)	Type of Material	Total Number of Cases	Number with Emboli	%
Scriba	General, autopsy	46	28	52
Carara	" "	102	28	26.4
"	Fractures, "	17	13	76
"	Heart, kidneys and vascular disease, autopsy	--	--	22
"	Burns, autopsy	--	--	44
Katz	General, "	600	194	32
Katase	" "	120	70	58
Lehmann	" "	50	37	74
Barack	Clinical, fatal cases	929	3	.32
Reiner	Operations	1000	4 (fatal)	.4
Utgenant	Orthopedic operations	4800	25	.52
Burger	Traumatic, autopsy	--	--	100
Deutsch	Fractures	2000	13 (fatal)	.65
Grohndahl	Fractures	1026	12 (fatal)	1.2
Killian	Surgical patients	70,000	112	1.6

Vance in 246 consecutive autopsies obtained the following:

	Total Number	Negative Results	Positive Results	Moderate or Severe	Fatal
Traumatic	164	62	102 (62%)	45	3
Non-traumatic	59	53	6 (12%)	--	0

Wright in 100 consecutive autopsies:

	Negative	Positive	Positive 2 to 4+
Non-traumatic	33	27	1
Traumatic	15	25	10

It is obvious that statistically the incidence varies enormously. In general autopsy material, the percentage ranges from 12 to 74%. In autopsy material from traumatic cases, the figures are from 25 to 100%. The incidence based on clinical data ranges from .3 to 1.6%. From these figures it has been deducted that fat embolism can be found in the organs at autopsy in the absence of trauma during life;

that it is much more common and extensive in cases of injury; and that clinically from .3 to 1.5% of the cases show symptoms from the condition. In the two large series of fracture cases between .32% and 1.2% have died from fat embolism.

The incidence within the same series has varied according to the type of cases admitted during that period. In Killian's group, fat embolism increased 4 to 5 times during the last few years, whereas the number of admissions were only doubled. The increase apparently was due to the greater percentage of severe accidents from various types of motors.

Etiology

Sex	Male	Female
Scriba	84%	16%
Killian	89%	11%

Age (Killian's collected cases ?)

	Fractures	Fat Embolism
Up to 10	6-19%	3.3
11 - 20	6-14%	16.1
21 - 50	47-59%	48.3 - 53.3%
Over 50	20-30%	27.5 - 36.5%

The peak according to age is between 30 and 50. The incidence before 20 is very appreciable. Several other authors state that the condition is uncommon before 20 and is increased in old age due to the greater fat content of the bones. Killian's figures do not bear this out entirely. This author stresses its occurrence before the age of 20.

Type of injury:

Traffic injuries		57
Railroad	6	
motors	36	
bicycles	3	
wagons	8	
Non-traffic injuries		
falls	25	
crushing injuries	7	
postoperative	7	
bullet wounds	2	
other injuries	4	

Area involved:

Femur, hip	32
ribs, sternum	30
tibia, fibula	25
base of skull	23
vertex of skull	18
humerus, elbow	14
organ injury	13
pelvis	13
vertebrae	12
below elbow	9
foot	7
shoulder girdle	5
facial bones	4

This table (Killian) is not accompanied by any statement regarding the frequency of each injury among general admissions. From another table, the following can be abstracted:

Bone injured	No. of Cases	No. of Emboli	Percent of Emboli
Leg	232	4	1.7
Femur	122	8	6.5
Arm	94	3	3.2
Forearm	73	1	1.4
Skull	62	8	13.0
Foot	43	1	2.3
Ribs	39	1	2.6
Shoulder	36	1	2.7
Vertebrae	29	3	10.3
Pelvis	13	4	30.7

The author does not comment on this percentage incidence per type of fracture. It is difficult or perhaps not justified to interpret the table. It does not correlate very closely with Vance's table except in case of fractures of the pelvis. Possibly the severity of the trauma is more important than the site of injury. This point has been stressed by other authors. Repeated injury, such as movement of fracture ends, mallet blows, forceful manipulations and similar continued injury is considered to be very important as an etiological factor. In Killian's group, 50 cases were due to multiple and 49 to single fractures. Warthin states that the degree of injury in some cases may be apparently slight.

Causes other than bone injuries (Warthin):

Surgical operations:
- Amputations
- Osteoclysis
- Manipulations
- Reductions of dislocations
- Resections
- Pressure on atrophic bone
- Use of chisel
- Concussion, etc.

Concussion without fracture
Acute periostitis and osteomyelitis
Hemorrhages into marrow
Foreign body in marrow
Soft tissue injury
- Crushing
- Inflammation
- Necrosis
- Operative procedures in fatty tissue

Rupture of fatty liver
Childbirth
Lipaemia due to disease (usually only at autopsy)
- Diabetes
- Pancreatitis
- Gout
- Anemia
- Nephritis
- Chronic disease of liver, pancrease, heart
- Generalized malignancy

Lipaemia due to intoxications
- Potassium chlorate
- Phosphorous
- Carbon monoxide
- Acute alcoholism
- Chloroform

Fatty degenerations
- Thrombi
- Intima of vessels
- Heart
- Cells in blood stream

Convulsive seizures
- Tetanus
- Eclampsia
- Delirium tremens
- Strychnine poisoning

Burns, especially of panniculus
Portogenous fatty embolism of liver

Pathology and Pathogenesis

The amount of fat liberated has been variously estimated. Warthin suggests 1 cc. per 1 - 2000 gm. body weight. Scriba stated 210 gms. was necessary for fatal fat embolism. Febiger reported a case of fatal embolism after injection of 50 cc. The work of Killian, Omanig and others shows that several factors are present: the rate of absorption, amount, nature of the fat and the condition of the heart. Small doses over short intervals act by summation and the result is like that of a simple large dose. A long interval between doses increases the total amount tolerated.

The source of the fat is generally assumed to be from the injured area. In some cases, the amount of fat in circulation seems out of proportion to the amount which could possibly be obtained from the fractured bone, e.g. from the patella or facial bones. For this reason, the suggestion has been advanced that there may be mobilization of body fat or some physical change in blood lipoids producing circulating globules of fat. The relatively high incidence of embolism after head injuries (Killian) suggests some possible injury to the fat regulating centers (verbally suggested by Dr. McQuarrie). In the absence of any proof of this possibility, the generally accepted theory is that the fat escapes from cells whose membrane has been ruptured by the trauma. The torn veins, held open by the surrounding bone "suck" the fat into the circulation. Continued motion, blows, severe trauma, multiple injuries are considered to increase the amount of liberated fat. Increase of tension in the marrow cavity, thru hemorrhage, edema or inflammatory exudate promotes the absorption of the fat.

Course of the fat is now conceded to be entirely by way of the blood stream, through the lungs, into the arterial blood and thus to the viscera and brain. The emboli in contrast to blood-clot

emboli can change their size (by elongation) and pass through capillaries. Therefore, it has been suggested that the stagnation of the fat in the lungs is dependent upon the force of the right heart. After passing through the lungs, every organ in the body is anatomically affected. The fat can be observed even in the retina. The histological change is that of any aseptic infarction of microscopic size. There is necrosis, edema and infiltration of blood. Soon, thereafter, a leucocytic reaction occurs. Phagocytes are especially numerous and most of these become laden with fat. In the lung, the areas involved usually are closely set since this organ is most involved. At times, the hemorrhagic exudation becomes confluent and large areas or entire lobes are involved so that a diagnosis of hemorrhagic (streptococci) pneumonia may be made. Non-specific "pneumonia" is the usual postmortem diagnosis. In the brain, the hemorrhagic infarcted areas appear as petechiae and this has been called "cerebral purpura" and has been confused with the "hemorrhagic encephalitis", such as is seen in some cases of arsphenamine reactions. In the serous surface, including the epi- and endocardium and the skin, the infarcted areas appear as petechiae. The skin of the shoulders, chest and arms seems to be characteristically affected. The fat is released from the infarcted areas and can be found in the sputum and in the urine.

Variations in the general picture may occur. Large quantities of fat suddenly released into the blood may act on the heart like a venous air-embolism. It may remain in the ventricle, stimulate the deposition of fibrin and produce an antemortem thrombosis of the right heart and vessels. Ikeda demonstrated such a process experimentally with the use of lipiodol. In the various organs, the lungs, brain and heart are most injured physiologically. Embolism of the heart muscle has been emphasized by Warthin. Since the stagnation of the fat, and hence the symptoms, are apparently dependent on the force of the heart beat, the weakening of the heart through infarction of its muscle becomes an important factor.

Clinical Features

In the older literature, two types were described: pulmonary and cerebral. Warthin would add a third or cardiac form. There is no anatomic basis for the division; it is a clinical differentiation dependent on the most manifest symptoms. This probably is quite arbitrary since the symptoms attributed to brain or lung involvement overlap to a considerable degree.

The onset may be immediate or, as is more common, after a free interval of a few hours. The free interval often is not seen (as in Killian's group) because this time is occupied by the transportation to the hospital.

In the pulmonary form, the following symptoms and findings are listed: Dyspnea, cough, cyanosis, pulmonary edema, restlessness, headache, increased pulse rate, low blood pressure, precordial or epigastric pain, irregular respiratory rhythm, increased pulmonary resonance, moist rales, dilated right heart, sputum sometimes blood streaked and later containing fat droplets and an elevated temperature. There is a wide range of severity of the symptoms. One group die very quickly in a state of collapse with a marked fall of blood pressure. These deaths usually are considered to be due to "shock" or "cardiac failure" and the diagnosis is established only after adequate postmortem examination. (Search for fat by proper stains) In other cases, rapid asphyxia and air-hunger develops and goes on to death. Such rapidly progressing types have been designated as "apoplectiform."

The cerebral form usually has a preceding interval in which the patient is free of symptoms. These begin as uneasiness, headache and restlessness. Finally mental cloudiness, hallucinations, delirium, loss of reflexes, clonic and tonic contractures of muscle groups, generalized convulsions, localized or extensive paralysis, stupor and coma develop. With these, there is a rapidly rising fever, rapid pulse, cyanosis, dyspnea and hypotension.

Warthin feels that many of the manifestations of vasomotor collapse are due to coronary emboli and designates these as the cardiac features.

This same author first pointed out the presence of fat in the sputum and since then this has been referred to as Warthin's sign. Before this, fat in the urine had been observed. Whereas, fat can be found in both these fluids in several other conditions and in itself is not diagnostic, its presence is a definite aid in conjunction with the other findings. These two examinations with examination of the eyegrounds for emboli, the skin for petechiae and blood serum for free globules of fat is given by Warthin as supplementary measures for diagnosis.

The temperature curve has been described as being subnormal. This apparently is an unusual circumstance; in most cases, the curve shows a rapid rise in both the cerebral and pulmonary forms.

The differential diagnosis often is very difficult. The conditions for which fat embolism is mistaken include shock, cardiac collapse, intracranial hemorrhage, hysteria, acute alcoholism, sunstroke or heat exhaustion and diabetic or uremic coma.

Prognosis cannot be estimated from the literature. Warthin and others believe that a large proportion of cases recover. The recorded mortality is extremely high because the diagnosis is not certain or is not made in the cases that recover.

Treatment

The recent literature indicates that many studies are being made to improve the treatment of this condition (see Ruckert). Various methods either to increase the body tolerance or to emulsify the fat have been tried and all have been unsuccessful. The only methods of treatment are those suggested several years ago by the earlier workers. All of these are prophylactic. Reduction of trauma by proper splinting during transportation, avoidance of unnecessary manipulation and modification of operative procedures to diminish trauma are considered to be the most beneficial. Of the more active measures, various forms of tourniquets to prevent aspiration, incision of the fracture site to relieve hemorrhage and free fat and venesection below the tourniquet before its removal have been suggested. Based upon the older idea that the fat enters the circulation through the thoracic duct, Wilms suggested making a thoracic duct fistula. This procedure is no longer to be considered since it is generally accepted that the fat travels entirely by way of the blood.

Impressions

1. Study of fat embolism dates to Magendie early in the 19th century. Zenker in 1862 described the first case of pulmonary fat embolism. In 1873, Bergman made the first clinical diagnosis. By 1931 about 200 articles were found by Killian and only 33 of these were written in any language but German. Warthin in 1913 collected only 15 American articles.

2. The incidence shows wide differences in the various series. Probably the greatest factor causing this variation is the interest of the investigator. This applies both to clinical and autopsy material. Another factor is the difference in the type of patient. These institutions receiving the seriously injured show the highest incidence.

3. In routine autopsy material, fat emboli are found in 25 to 75% of cases. In autopsies performed on accident cases, the percentage ranges from 25 to 100%. The degree of embolism is variable. In the traumatic group, it is estimated that 35 to 40% show moderate or severe embolism. In the non-traumatic group, the degree of embolism usually is slight and possibly is of no clinical significance.

4. In contrast to this high incidence in autopsy material, the incidence based on clinical findings is very low and ranged from .5 to 2%. The belief has

been expressed that this low clinical incidence is due to a failure of recognition.

5. In two large series, the percentage of males was 84 and 89%., respectively. This was not correlated with the male-female ration of admissions of accident cases.

6. It is frequently stated that the incidence increases with age because the bones show an increase of fat content as they become older. This is not borne out by Killian's statistics which show a greater incidence before 20 than after 50. The peak in all series is between 20 and 50.

7. In a group of 112 cases, 105 were due to injuries and 7 were postoperative. Of the injuries, 50% were due to various forms of traffic accidents and 25% were due to falls.

8. The area involved listed in order of frequency is as follows: femur and hip (32 cases); ribs and sternum (30 cases); tibia and fibula (25 cases); base of skull (23 cases). Attempts to correlate this with the frequency of injuries to the same areas are unsatisfactory. In one group, an attempt at such a correlation gives the following order of frequency: pelvis (31%), skull (13%), vertebrae (10%), femur (6.5%), arm (3%). In another series, the results were considerably different with the exception that the pelvis again headed the list. Probably the severity of the trauma and the amount of movement after the fracture are more important factors than the site of the injury. In one group, 50 cases were due to multiple and 49 to single fractures. In some cases, the degree of injury seems to be very slight.

9. A wide range of conditions other than fractures have been reported as the cause of fat embolism. The most important of these are the various surgical operations on bone involving pounding, osteoclysis or manipulation of joints. Other conditions are: soft tissue injuries or operations, concussions, acute infections in bone or fatty tissue, and conditions that might increase the intermedullary pressure, such as hemorrhage. In the non-clinical type of fat embolism, the various forms of lipaemia associated with disease, for instance diabetes or due to intoxications such as phosphorus or carbon monoxide poisoning have been described.

10. The amount of fat necessary to produce clinical symptoms of fat embolism varies according to the different authors from 1 cc. per 1000 grams of body weight to a total dose of from 50 to 200 gms. Apparently the rate of absorption into the blood, the total amount, the nature of the fat, and the condition of the heart muscle are important factors. Small doses occurring within short intervals produce the same results as a single massive dose.

11. The source of the fat is assumed to be from the injured area. Since in some cases the injury appears to be trivial, it has been suggested that there occurs some physical change in the blood lipoids, or some change in the central nervous system allowing absorption of fat globules from the subcutaneous deposits. These theories have not been substantiated by experimentation.

12. The fat is carried by the blood to the lungs and since the globules can change their diameter by elongation, they can be forced through the lungs into the arterial blood and are then dispersed to all of the organs. As far as can be determined, the lungs, brain and heart are the only organs whose function is altered by the emboli.

13. The stoppage of the globules in a capillary produces a minute infarction with edema, infiltration of blood and necrosis. In the lung, the hemorrhagic exudation becomes confluent and the gross and microscopic appearance is that of a hemorrhagic (streptococcic) pneumonia for which it is usually mistaken. These infarcted areas may become secondarily infected from the bronchi. In the brain, the multiple infarcted areas have been described as "cerebral purpura" and the condition has been confused with forms of hemorrhagic encephalitis. The infarctions

ppear in the skin as petechiae, especial-
y about the upper part of the body. The
'at making up the embolus is taken up by
hagocytes (?) or escapes by some other
eans and can be found in the sputum and
rine. Such occurrences are considered
o be of diagnostic importance.

14. Warthin has emphasized the impor-
ance of the heart in the production of
he clinical symptoms. Stagnation of the
mboli, particularly in the lungs, is
.ependent on the force of the heart. In-
'arction of the myocardium creates a
'icious circle and this author believes
hat death is frequently due to cardiac
'ailure rather than primarily to the pul-
ionary or cerebral injury.

15. The symptoms are usually a combina-
:ion of the results of pulmonary, cardiac
nd cerebral infarction. The onset may
:e immediate and rapidly progressive
(apoplectiform) or more commonly after
a free interval of a few hours.

16. The signs and symptoms attributed
:o cardiopulmonary injury are: dyspnea,
:ough, cyanosis, pulmonary edema, rest-
.essness, headache, elevated pulse rate,
ypotension, precordial or epigastric
pain, irregular respiratory rhythm, in-
:reased pulmonary resonance, moist rales,
dilated right heart and fever.

17. The changes attributed to cerebral
injury are: headache, restlessness, hallu-
:inations, delirium, clonic and tonic
:ontractures, convulsions, mental dulness,
loss of reflexes, localized or general-
ized paralysis, stupor and coma. Usually
there is a combination of the cerebral
and cardiopulmonary symptoms.

18. The differential diagnosis often
is difficult. The conditions for which
fat embolism is mistaken includes shock,
"cardiac collapse," intracranial hemor-
rhage, hysteria, alcoholism, sunstroke
and diabetic or uremic coma.

19. Warthin suggests the following
points in making a diagnosis in addition
to the history of trauma of symptoms:
fat in the sputum and urine, fatty emboli
in the retinae, petechial hemorrhages in
the skin, and free fat globules in the
blood serum.

20. The mortality from fat embolism
cannot be estimated from the literature.
Some authors believe that a large number
of undiagnosed cases recover.

21. Active treatment of the condition,
when clinically evident, is poor. Ex-
periments have been recently conducted
to change the physical property of the
fat and make it more tolerable. These
have been unsuccessful. Treatment of
the low blood pressure is considered
to be important.

22. Prophylaxis is probably of
greatest value and consists chiefly of
immobilization during handling of
fractures and modification of operative
procedures to diminish trauma. Other
methods suggested by some authors are:
incision of the fracture site to eva-
cuate blood and fat, tourniquets to pre-
vent aspiration, venapuncture below the
tourniquet and incision of the thoracic
duct?

R. W. Koucky

II. CASE REPORT

CHRONIC HYPERTROPHIC ARTHRITIS; FAT EMBOLISM

Case that of a white female, 14 years of age, admitted to the University Hospitals 9-7-33, expired 11-4-33 (58 days).

Progressive Arthritis

6- -29 - Developed soreness in knee which progressively became worse and rapidly involved all joints, including opposite knee, elbows, ankles, wrists, fingers, toes, shoulders, neck, etc. After several months, progressive pain and stiffness, and fusiform tender swelling appeared on each joint. Swellings never red or tense. Pain severe for about one year. Aggravated by motion. Subsided after one year (3 years prior to admission) and did not occur again. When patient recovered from pain, all joints presented fusiform swelling and limitation of motion. Stiffness progressively became worse until motion almost entirely lost in all joints.

Admitted

9-7-33 - Physical examination: Elbows, wrists, knees, ankles and ankle joints all show fusiform enlargement and marked limitation of motion; other joints stiff, including neck. Enlarged joints firm, no redness but bluish. Heart - enlarged, no murmurs. Generalized adenopathy. Tongue mottled with white exudate; gums inflamed and bleeding. Diagnosis: Chronic hypertrophic arthritis. Vincent's infection of mouth.

Laboratory

Urine - negative. Blood - Hb. 72%, rbc's 3,740,000, wbc's 8,250, Pmn's 73%, L 26%, E 1%. Smears from mouth - positive for Vincent's organism. Treatment: Traction applied from Balkan frame to gradually extend the knees.

Operation

10-2-33 - Ham string tenotomy done and a posterior splint applied to prevent foot drop.

10-18-33 - Condition not improved sufficiently to allow patient to walk.

Second Operation - Immediate Onset of Symptoms

11-4-33 - Bilateral posterior capsulotomy performed. Returned from operating room at 10 A.M. Condition fairly good. During the operative procedure the left tibia was fractured. Almost simultaneously with occurrence of fracture, anesthetist noted that patient's breathing became different and pulse became elevated. Condition of patient poor. Subcutaneous fluids immediately postoperative. 12:45 P.M. - Appeared to be in surgical shock. Intravenous fluids started. Blood transfusion given. 1:15 P.M. - No improvement. Appears to be in typical surgical shock. More blood given. 1:30 P.M. -Expired.

Clinical Diagnosis: Fat Embolism.

Autopsy

The body is that of undernourished and underdeveloped, 14 year old, white female. Rigor cannot be determined because of the marked stiffness of all the joints. The joints are held in a partial flexion. There is a fracture of the head of the tibia and fibula on the left side. There is a recent operative wound on the lateral and posterior surface of the ends of the femur over the back of the knee joints. No cyanosis or jaundice. The pupils are equal, each measuring 3 mm. in diameter. Subcutaneous fat is scanty. There are no other special marks.

The peritoneal cavity contains no excess fluid. No petechiae seen in serous surface. The appendix hangs free and shows no inflammation.

The pleural cavities contain no excess fluid, adhesions or petechiae. The pericardial sac is completely obliterated but the adhesions can be easily separated with the fingers.

Petechiae in pericardium and endocardium

The heart weighs 200 grams. No apparent hypertrophy of the musculature is seen. No dilatation of the cavity. There are numerous petechiae seen in both the pericardium and endocardium. The mural endocardium is smooth. The musculature shows no fibrosis or softening. There is no evidence of recent or old endocarditis of the valves. The root of the aorta has a good caliber. The coronaries are not examined.

Lungs Apparently Normal

The right lung weighs 240 grams, left 190. The posterior surface of the right apex shows a nodule measuring about 2 cm. in widest diameter which resembles infiltration of the lung parenchyma with blood. The nodule is fairly well circumscribed and moderately firm. On cross section, there is no softening at any point. The remainder of the lung tissue appears entirely normal.

The spleen weighs 75 grams, appears to be normal. The pulp has the usual markings and is not particularly soft.

The liver weighs 750 grams. The liver markings are well retained. The periportal spaces show no fibrosis. No abscesses present.

The gall-bladder has a thin wall and contains no stones. The ducts are well formed.

Gastro-Intestinal Tract shows no ul-

usual adhesions. No malformation, ulcerations or localized areas of inflammation.

The pancreas is soft and pink, contains no tumors or cysts.

The adrenals are well-developed, show no adenomas or degeneration.

Pyelitis

Each of the kidneys weigh 100 grams. The capsules strip easily. The kidney substance is well demarcated in cortices and pyramids. On the right side, some pus is present in the pelvis of the kidney and the mucous membrane of the pelvis shows some thickening.

The bladder shows very definite cystitis, manifested by trabeculation, thickening of the mucous membrane and discoloration.

Genital Organs: are of the usual infantile type. Ovaries show no follicles. Uterus is usual size for a 5 to 8 year old girl. No adhesions.

Neck - not dissected.

Questionable Petechiae in Brain

Head: The scalp, calvarium and meninges show no noticeable change. Cerebrospinal fluid is clear. The arachnoids and pia show no thickening or accumulation of pus. The convolutions of the brain are well marked. The ventricles are not dilated. The choroid plexus shows no change. The brain is sectioned in rather thin serial sections and carefully examined for the presence of petechiae. In occasional areas, a small reddish spot is seen which resembles mostly a dilated or injected blood vessel but several of these areas could not be wiped off and might possibly be petechiae. Nothing resembling the usual picture in fat embolism of the brain can be demonstrated.

Microscopic

Massive Embolism; No Infarction

Organs of the lung and brain from various places are cut, frozen and stained for fat. The lung presents a remarkable appearance. It appears that every capillary within the alveolar walls is distended with fat. The alveoli are open and there is no exudation of blood into the alveoli. In the sections of the brain, fat can be very easily found in the small capillaries in almost every section. Again, no exudation of blood can be seen.

Diagnoses:

1. Chronic hypertrophic arthritis.
2. Capsulotomy of both knee joints.
3. Fracture of tibia and fibula.
4. Fat embolism, generalized.
5. Questionable petechiae in brain.
6. Petechiae of epicardium and endocardium.
7. Adhesive pericarditis.
8. Pyelitis, right kidney.
9. Cystitis.

III. PAST MEETINGS

MEETING OF STAFF

Date: March 1, 1934

Place: Recreation Room, Nurses' Hall

Time: 12:18 - 1:20

Attendance: 118

Program: Actinomycosis

Discussion: L. G. Rigler
R. W. Koucky
A. T. Henrici
C. P. Fitch
W. L. Boyd
O. H. Wangensteen
K. W. Stenstrom

Theme: L.G.R.: Large number of examinations on this boy. Colon showed downward displacement characteristic of enlarged liver. Note outline of spleen pushing flexure down. Chest showed pleurisy with small amount of fluid. Some idea of ramifications of the injected sinus can be made out (very small cavity). Because of suspicion of something in the liver films made after thorotrast. Note diffuse mottling and enlargement. Definite diagnosis of multiple abscesses made at this time, also some destruction in 3 of the ribs.

Later developed considerable effusion on the left side, small amount on right. It is a little difficult to see but in the 12th rib posteriorly some involvement is shown. 7th is distinctly eroded and the anterior part very much destroyed. Rest of films show progression of lesions.

R.W.K.: (Dr. Randall's slides) Colored plate. This is characteristic histological appearance of imbedded granules. This is much greater magnification of an earlier lesion. Note colony in the center. Center of granules is a large mass with superimposed pus cells. Note young fibroblasts beginning to form, dense fibrous reaction. Here is an older lesion, same type of process near the granule but the peripheral areas show dense fibrous tissue characteristic of this stage. Sometimes biopsy shows heavy fibrous tissue and miliary type of abscesses. Colored plate showing large clear cells.

A.T.H.: I still think the best way to diagnose actinomycosis is to look for granules in the pus. I have had several cases where we could not find granules in the pus by the usual bacteriological procedures where the pathologist picked them up in biopsies. I cannot see what can be gained by cutting sections of the pus. You are only seeing small amount of pus. If you take your pus, dilute it with water and saline, spread it out in thin layer you can examine all the pus.

Cultures. You find it generally stated in the literature that serum is necessary for growth. I do not believe that any more. We have been making cultures from good many cases. Serum is not necessary. It is difficult to isolate organism in cultures, not because it is hard to grow but due to heavy overgrowth of secondary bacteria. While it is difficult to isolate it is not difficult to get growth. Organism is not strictly anaerobic. Simple anaerobic methods will suffice. You get the development of colonies within about a week. Colonies once recognized are striking and characteristic.

In regard to the geographic distribution, based on figures calculated on total number of cases per state without consideration of density of population, the disease is very distinctly prevalent in the upper Mississippi Valley.

I believe more likely to make progress in study of this disease by paying attention to allergic phases. As I see these fungus infections I am struck with the similarity from the clinical standpoint between tuberculosis, actinomycosis, and other fungus infections. Miss Harrison working in our laboratory, got interesting and confusing data. She used antigen in skin tests. Few cases of actinomycosis. Practically all normal cases gave marked reaction. Some people were extremely sensitive to this antigen. When we tried it on cases of actinomycosis all but one gave completely negative reaction. One gave very weak reaction. When it came to guinea pigs we found reverse. Normal guinea pig was not sensitive to extract but following a second injection we got some necrosis and formation of subcutaneous abscesses. One of the great difficulties in studying actinomycosis is difficulty in producing it in experimental animals. The results are not uniformly positive by any means - at least this has been my experience. In skin tests we got abscesses with the dead cultures. We started inoculating them with living cultures and succeeded in producing actinomycosis. It looks to me as though allergy plays a large part in the development of this disease. Cannot produce disease in guinea pig in usual way. In European literature there are often reports on treatment with vaccine. I am skeptical about value of vaccine in the treatment of any disease.

C.P.F.: Actinomycosis in animals is a relatively common disease. Our knowledge has changed considerably in the last 3 years. We always believed up to the time of Dr. Thompson's article that the fungus was responsible. Now we know it is the actinobacillosis. In other words, actinomycosis of Wolff-Israel type not as common as actinobacillosis. There are 3 conditions in animals which may be confused;
(1) We see chronic abscesses with granules commonly in aged sows, also horses

(streptococci, etc.) - very common. (2) Wooden tongue now quite common, is almost entirely actinobacillosis; and (3) True actinomycosis (a rare disease).

W.L.B.: We treat jaw surgically in animals. Formerly we attempted to use potassium iodide, particularly in wooden tongue. Good results, but the disease occurs largely in the region of the head and neck and wherever possible we treat by removing all the diseased tissue possible, then use the cautery.

O.H.W.: Showed patients with actinomycosis which were treated last few years. There still persists in literature the impression that actinomycosis is hopeless disease. Dr. Henrici has many times said that actinomycosis is due to exogenous organism. Actinomycosis generally exhibits unusual tendency to heal. Portal of entry is mouth or cecum, and often times when seen actinomycosis of right lower quadrant is found. It presumably comes from the cecum. In the neck it dissects down to the thorax. Occasionally cases seen in the urinary tract.

(Patients shown). In 1930, patient came to us with lesion outside of face. Large granulomatous appearing mass side of face. Aspirated with needle and found fungus. Disappointed with previous treatment. Lesion excised. No other treatment given. Now well and opens mouth fairly widely.

Other similar case. Had actinomycosis for 2 or 3 years. Lesion in neck, cheek, and below ear. I excised this somewhat widely.

Another patient. Lesion treated with x-ray elsewhere. Excised lesion. Both well today.

In this girl, only thing we did was 2 curettements. Introduced curet through sinuses. No other treatment. Now patient presents herself with no actinomycosis. About follow-up, it is my conviction that if the skin is healed actinomycosis is cured. This is the method by which we are treating actinomycosis at present time. Condition exhibits unusual tendencies to heal.

This patient (slide) with thoracic actinomycosis, had 4 operations. Has had several recurrences since but the actinomycosis localized. Will be cured ultimately with curettements. X-ray treatment given. Here is another patient. Came here short time ago with large abscess over face. Has been treated like the others. Opened the sinuses, curetted them. It is my impression that when the skin is healed, disease cured. I do not believe any radical surgery is necessary. I don't believe it will be necessary in abdominal actinomycosis. I can show you cases of abdominal actinomycosis cured by abdominal curettement only. In pulmonary and abdominal actinomycosis, this can be done by relatively simple measures. Does not require radical surgery. No one can deny value of x-ray treatment. I am convinced that potassium iodide is of no value. I know that surgical drainage will cure actinomycosis. X-ray exhibits no effect on the organism.

K.W.S.: Distinction between thoracic and abdominal and fascial type. The first patient that I had a chance to treat was a prize bull. Wanted to keep him going for another year. One of the first cases that we had here was a very bad one with multiple lesions. Impossible to do surgery. Treated one area with heavy dose. Left him alone for a while, then we could see distinct difference. Started to clear up in the area. We continued with treatment and after a while went home. He refused to come back to the hospital. We had about 4 cases of thoracic and abdominal and those 4 are dead. We do not have much hope for them. We have had 3 fascial types without incision and all did well. I believe that if it is too much for a surgical curettage, we should treat patients with x-ray. I do not believe incision alone would cure cases.

Gertrude Gunn
Record Librarian.

MEETING OF STAFF

Date: April 5, 1934

Place: Recreation Room, Nurses' Hall

Time: 12:20 - 1:16

Attendance: 121

Program: Hemangiomata

Discussion:
L. G. Rigler
R. W. Koucky
J. F. Madden
C. E. Rea
C. O. Rice
O. H. Wangensteen
K. W. Stenstrom
H. E. Michelson
Laura Lane
W. T. Peyton
R. C. Gray
L. G. Rigler

Theme: L.G.R.: Hemangiomas interesting to roentgenologists. Many picked up more or less accidentally. In this case, while studying chest, rib tumors discovered. Further studies showed other tumors in pelvis, femora and skull. Intravenous urography was negative. Striking feature is irregular destructive character of tumor. Some areas of new bone. Multiple character and its obviously malignant character. All of these suggested some type of endothelioma or myeloma.

(Other cases shown). This is a classical picture as seen in spine. Body of vertebra mushroomed out with dense trabeculae running vertically through bone. Big one like this strikingly obvious and may give rise to some symptoms. Another case, showing trabeculae not nearly as marked, involving the 4th lumbar vertebrae. Tendency to collapse of vertebra and trabeculae well shown. Characteristic feature.

R.W.K.: Only 2 slides - one bone, one liver, other tumors approximately same structure. Heavy fibrous stroma. Large spaces filled with blood. Endothelioma throughout the entire tumor shows no proliferation. Thin nuclei, smooth, not malignant. Stroma composed of collagenous material, takes azocarmine stain. No elastic fibers. Blood vessel walls imperfectly formed. Same type of structure in the liver. Brings up question whether metastatic or primary in the liver. Appearance suggests latter. This operative specimen illustrates hemangioma in the tongue. Another one from cervix looks like extensive telengiectasis rather than tumor. Have several specimens from case that came to autopsy recently. Lesion in kidney pelvis is a simple dilatation of capillary bed. Same in the specimen from bladder. In the cecum and stomach same type of lesion present but in addition small star-shaped hemangiomas. Stomach shows over 40 star-shaped hemangiomas. Liver shows generalized enlargement of spaces. Lesion in auricle of heart, the nature of which we are not yet sure. Small oval, yellowish bodies, cystic, contain thick yellow material, look like pus. So far, tentative diagnosis is lymphangioma of auricle.

J.F.M.: I haven't anything to add except from what we learn from our own cases. Slides shown: First is that of the nevoid type of telengiectasis showing grouping around umbilicus. Also in other organs because x-ray examination of skull showd erosion of the inner table. Constant headaches. We thought he must have had accompanying telengiectasis probably in the meninges. Next shows lesion on the bulbar conjunctiva. Also case with lesions on penis. (Next): First example of Osler's disease we saw. Patient 50, repeated hemorrhages over almost all of her life. Epistaxis as often as 8 or 9 times day. Hemoglobin, 97%, normal red count. Resembles the case recently autopsied. Other patients at autopsies bring out the point that number of telengiectasias on the skin have no relation whatever to the number of telengiectatic lesions in other organs. May be very marked involvement of all the internal organs.
(Next): Generalized telengiectasia and chronic myelogenous leukemia. In this type as soon as the constitutional

disease is overcome ordinarily the telengiectasia disappears. Here the cause not removed and telangiectasias are increasing. (Next): Nevoid type of telengiectasis associated with papillary melenotic lesion.

C.E.R.: Should be emphasized that not all hemangiomas are malignant, some are benign. Inasmuch as they are undifferentiated malignant nature justified. Microscopically hemangiomas are lobular, composed of undifferentiated cells inside the wall. Others are benign. This tumor brings out importance of taking into consideration the clinical and gross features. This tumor presented today microscopically benign but clinically malignant. The outcome of the hemangio-endotheliomata in the skin is good. Difficulty in removing tumors in the muscle because of infiltration. On the skin probably best treatment is excision. If rather extensive or on face, cosmetic result is better by x-ray treatment. In muscle or other organs, probably the combined use of x-ray and surgery best form of treatment.

C.O.R.: The patient with tumor in thyroid had tremendous amount of bleeding at the time of operation. Given x-ray therapy, recovered. Well year ago when last seen. No evidence of recurrence. Cases in Europe operated upon, x-ray not attempted and large proportion fatal. X-ray therapy large factor in the therapy of this type of case.

O.H.W.: In case Dr. Rice referred to, it was difficult for me to see why there was so much trouble in stopping bleeding until I started to help with the operation. We haven't much experience with the injection of sclerosing solution. Many hemangiomas represent abnormal arteriovenous aneurism. Presence of arterial blood in the veins aids in making diagnosis. We have been interested in this condition in the extremities.

K.W.S.: We haven't had so much experience with the more serious conditions described. Great number of benign types in children in skin. Local response to irradiation very good. Give a rather small dose, wait 6 weeks, then give second treatment. Some do not respond to first treatment but respond nicely to second. Gradually improve and completely disappear. In older people they do not respond as well. Radium said to be better than x-ray. No difference in our experience with some very large lesions. One involved complete thigh in youngster 2 years old. After 2 treatments disappeared completely except small area left. We have treated couple of cases where there have been metastasis. One boy had involvement of scapula. Dr. Peyton did a radical operation. Later there was involvement of the chest, and that responded to radiation.

H.E.M.: One thing I would like to mention is the treatment of birth marks. Wrong to wait, the earlier the better, even first week in life. I want to warn also against birthmarks occurring at mucocutaneous juncture. Advise consultation because results are not what expected. Important to have someone else see it with you. About the treatment: If not getting results with treatment instituted, not well to push this form too far. Change to another type. Large pigmented nevi (port-wine stains) are job for plastic surgeon. Mistake to use radium, freezing, etc.

L.L.: I think one mistake that ophthalmologists make is not considering possibility of brain lesion. Hemangiomas in children on the lids respond very well when taken early. Better results obtained early. Another type we fall down on is the type near ala of nose involving cheek. Frequently forget to look in the nares to find involvement. Two of these cases in which operation had been done showed larger lesions inside nose. After the use of radium growths became quiescent. No sign of recurrence after 3 years.

W.T.P.: We carry out suggestion Dr. Michelson made. Last week we had one that was radiated twice, improved some, but did not get better. Different method probably will give good result. You cannot constrict the venous flow from the area so that fluid probably does not stay in lesion long enough to sclerose it but we have had quite a few successful results with injection treatment, especially in scalp. In this case Dr. Stenstrom

mentioned, biopsy diagnosed as fibrosarcoma. Later changed to hemango-endothelioma. In another instance, I operated upon a tumor and it was diagnosed as hemango-endothelioma. Then later in publishing case in connection with other material diagnosis was changed to myeloma. Apparently this group of tumors confuses the pathologists.

R.C.G.: Interesting in regard to diagnosis of localization of brain lesions is the injection of 10 cc. of thorotrast into the carotids.

L.G.R.: There have been some untoward results in the method. We have never tried it here.

Gertrude Gunn, Record Librarian.

IV. ANNOUNCEMENTS

1. SURGERY SEMINAR

Dr. Arthur A. Zierold will speak at the Surgery Seminar today, at 4:30 in Todd Amphitheater. Subject: Head Injuries. Anyone interested is cordially invited.

2. RADIOLOGY SEMINAR

"Details in the Roentgen Diagnosis of Brain Tumors" by Dr. John D. Camp of the Mayo Clinic, University Hospital X-ray Department, room M-515, Friday, April 13, at 5 P.M.

Dr. Camp will also speak in the Eustis amphitheatre at 3 P.M. Friday on "The Value of Roentgen Examination in the Diagnosis of Intracranial Tumors."

Anyone interested is welcome.

3. THE MINNESOTA PATHOLOGICAL SOCIETY

The University of Minnesota Medical School, Institute of Anatomy, Tuesday, P.M., April 17, 1934. The pathogenesis of the various forms of glomerulonephritis -- Dr. E. T. Bell. Sudden death in heart disease -- Dr. M. H. Nathanson.