

of embryonal cells, closely packed without any interstitial substance. The majority of the cells are round with large nuclei. Some are oval and many show two prolongations at the poles.

CASE III. Schwalbe<sup>3</sup> reports a case in a woman of twenty-three. Autopsy shows large tumor, filling up whole of left pleural cavity. Section through tumor shows that left lung is surrounded by the growth. Surface of tumor smooth, reddish yellow and of firm consistence. Tumor consists of greatly thickened pleura, 4 cm. in thickness. Cut surface grayish-red in color. Fibrous structure in which there are many cells, round and spindle-shaped. Bronchial glands enlarged. Metastasis in left lung, right eye, diaphragm and liver.

CASE IV. Leube<sup>4</sup> reports a case in a man of thirty years of age. Diagnosis established at autopsy.

CASE V. Stewart and Adami<sup>5</sup> report a case in a man thirty-four years old. Autopsy shows a soft mass extending from upper extremity of left thorax down to level of sixth rib. Upper part of growth firmly attached to costal pleura. Below where the border is free, the wall of the tumor is thick, dark blue in color, resembling a cyst containing blood. Heart displaced downwards and to left. The mass of tumor is very soft and on breaking capsule a large amount of semi-solid material of a dark purplish color easily passed out through the opening, about fifteen hundred cubic centimeters in all. The appearance is that of soft, breaking down blood clot. The mass is closely connected with the lung but no actual communication is demonstrable. Tumor thought to have started in a sac left after old adhesions. Microscopic examination shows lower mass almost pure blood clot. Denser parts show lobules of sarcomatous tissue. Many greatly dilated vessels of embryonic type in the denser tissue with very delicate walls. Cells are oval with oval well-staining nuclei separated in places by extravasation of blood. The costal pleura has undergone great fibroid thickening and infiltrated throughout with sarcoma cells.

CASE VI. Kidd and Habershon<sup>6</sup> report a case of myxosarcoma in left pleura in a girl of eighteen. Autopsy showed an enormous mass filling left thorax; heart lying entirely to right of middle line. Pleural cavity almost entirely obliterated by soft spongy adhesions. Left lung displaced backward and almost entirely hidden. When the mass was removed it was seen to be a somewhat lobulated growth loosely attached to left upper lobe of lung and more firmly to lower lobe. The whole tumor is covered with a thin pleura-like membrane. On section the tumor is shown to consist of coarse fibrous network enclosing large blood cysts. Cystic spaces contain viscid puriform material and toward sternal border there are a few soft yellowish-white masses of growth. The blood cysts which were a predominant feature of the growth contain fluid and coagulated blood. The softened puriform material on microscopic examination proved to consist of stellate and pyriform cells. Some sections show coarse fibrous net work enclosing red blood corpuscles in its meshes and many large thin-walled vessels filled with blood. In its more solid parts the growth is composed of closely packed round cells with very scanty stroma. Many of the individual cells contain clear rounded spaces or drops, apparently the result of mucoid degeneration. Many branching cells are seen with clear mucoid drops in them. No metastasis in any other organ.

CASE VII. Finlay<sup>7</sup> reports a case in a man sixty-seven years old. Autopsy showed bloody fluid in left chest. Left pleura easily stripped from chest wall. Both layers thickened, 5 mm. in thickness. Inner surface studded with nodules of white or reddish color, which on section are uniformly white and juicy. The

nodules are from 5 mm. to 30 mm. in thickness, 8 to 60 mm. in diameter. Left lung is collapsed. One bronchial gland slightly enlarged, no metastasis in other organs. Microscopic examination shows the tumor to consist of large irregular-shaped, multinuclear cells with smaller round and oval cells between. Stroma not evident. Blood channels visible between rows of cells. Diagnosis, myeloid sarcoma.

CASE VIII. Kaufman<sup>8</sup> reports a case in a woman of twenty-nine years, where sarcoma, the size of a child's head, of soft consistency, was found in the right pleural cavity in the lower part. The diaphragm was involved in the growth. Microscopic examination showed a polymorphic cell sarcoma. The cell masses were arranged like mantels around wide thin-walled vessels. The vessels in many places were thrombosed and the tumor tissue was necrotic in many places. Small metastases in spleen, kidney and liver.

CASE IX. Oelrick<sup>9</sup> reports a case in a man fifty-nine years old. Autopsy shows left lung pushed up to top of thoracic cavity entirely above third rib. Heart pushed to right beyond median line and the rest of the cavity taken up by a great sac formed by the pleura, which contained about three liters of a dark reddish semi-fluid material, which in lower part is more of a yellowish color and very sticky. The parietal pleura is greatly thickened and covered with nodules of tumor tissue and is infiltrated throughout with tumor cells. Microscopic examination shows growth to consist of a mixed cell sarcoma. The left lung contains metastases and there are metastases in pericardium, heart, right lung, liver and both kidneys.

CASE X. Busse<sup>10</sup> reports case in a man forty years old. Autopsy showed the right thorax filled with an enormous growth. The tumor is firmly fastened to the chest wall. The lung is completely surrounded by the growth. The growth consists of very thick pleura, one to three cubic centimeters on section. The inner surface showed rounded nodules, some of which are 10 cm. in diameter; in places the tumor is as hard as cartilage; in places there is calcification and also in many places softening with cysts in which there is myxomatous material. Upon section the tumor has a honeycomb structure. The septa are firm tissue in which are blood vessels. The tissue between the septa is made up of cells lying in a very homogeneous substance resembling hyaline cartilage, and with its consistency. In other places the tumor is softer and has the character of myxomatous tissue. The cells are round or oval with large nuclei and easily staining protoplasm.

Diagnosis: Chondro-myxo-sarcoma.

#### REFERENCES.

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- <sup>3</sup> Schwalbe: Deut. med. Wochenschr., 1891, 1238.
- <sup>4</sup> Leube: Spec. Diag. inner. Krankh., 1891, 166.
- <sup>5</sup> Stewart & Adami: Montreal Med. Jour., 1894, 909.
- <sup>6</sup> Kidd and Habershon: Tr. Path. Soc., London, 1897, xlix, 15.
- <sup>7</sup> Finlay: Pract., London, 1897, 153.
- <sup>8</sup> Kaufman: Lehrbuch der Spec. Path. Anat., Berlin, 1901, 237.
- <sup>9</sup> Oelrick: Nord. Med. Ark., 1903, 6.
- <sup>10</sup> Busse: Verhandl. d. Deut. Path. Gesellsch., 1906, x, 171.

### GENERAL STREPTOCOCCUS INFECTION THROUGH UNRECOGNIZED CHANNELS: A REPORT OF TWO CASES.

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STREPTOCOCCUS septicemia is not apt to be considered in the differential diagnosis of a case which does not present signs of local sepsis or chronic wasting disease. The following cases are

presented to show the diagnostic importance of streptococcus septicemia in cases of obscure and severe infection.

**CASE I.** W. W. F. was admitted to Dr. Fitz's wards in the Massachusetts General Hospital on Jan. 11, 1908, and gave his history as follows: He was an American, white, thirty years of age, married, a waiter by occupation.

**Family history:** Father died at sixty-three of Bright's disease. Mother died at fifty-four of asthma and bronchitis. Wife and three children well. Two children died in infancy. One other child died of trauma. No history of consumption.

**Past history:** He remembered no past diseases excepting gonorrhea ten years ago. He had concussion of the brain several years ago after being kicked in a gymnasium. Appetite, sleep, bowels, micturition, normal.

**Habits:** Five cups of tea a day. No coffee, little alcohol. Seldom smokes.

**Present illness:** Seven days before entrance he went to bed at night feeling well. He awoke at 3 A.M. in a chill, shivering so that he shook the bed. During the remainder of the night he had frequent chills, but he did not feel feverish or sweat. He remained in bed until noon, when he rose feeling almost well. The following morning he went to work, but he soon fainted. He was brought home and put to bed where he remained. Two days before entry he rose from the bed and fainted. For five days before entrance he had felt feverish. He had no cough, sore throat, pain in chest or vomiting. Bowels were constipated for a few days. Urine dark in color. On the morning of the day of entrance he had considerable tenderness and some pain in his left lower leg.

**Physical examination:** The patient entered the hospital with a mouth-temperature of 100.4°, a pulse of 104, and respiration of 20. He was abnormally alert, slightly delirious, and talkative. He was willing to lie quietly in bed and was able to give his own history. All his motions were tremulous.

He was well developed and nourished. His skin and mucous membranes were moderately pale. His skin was hot and he perspired freely. His pupils were equal and reacted to light and distance. His tongue was dry and clean in the anterior portion, coated and white in the posterior. The pharynx was dry and bright red. Teeth good, several missing.

His heart was normal in size, and the sounds were of fair quality, regular and rapid. No endocardial murmurs. The radial pulse was regular, rapid, of small volume, and of very low tension. Artery wall was not palpable.

The lungs were normal.

The abdomen presented nothing abnormal. Liver and spleen were not made out to be enlarged.

He had slight hypospadias. His knee-jerks were normal. The plantar reflexes were not obtained.

Scattered over his extremities were the following lesions. The extensor surface of his right upper arm was red, swollen and tender. The circumference of the right upper arm was 10½ in.; of the left, 9½. Just below the external condyle of the right humerus was a fluctuant swelling 1½ in. long, not red or tender. Just below the right elbow on the inner surface was a dark brown, slightly tender spot, ½ in. in diameter, surrounded by diffuse swelling and tenderness, extending 3 in. below the spot and up to the elbow. There was a similar small brown spot 3 in. above the right elbow on the extensor surface. Over the right ulna, just above its middle, was a red, firm, tender swelling half an inch in diameter. On the back of the right hand from the

wrist to the middle finger was a red, slightly tender, fluctuant swelling 2 in. wide. The fingers and wrist can be moved with slight pain. On the back of the left hand near the wrist was a red, fluctuant swelling 1 in. in diameter.

On the right buttock near the thigh was a flat reddened area half an inch in diameter and slightly tender. Just above the right popliteal space was a similar spot, which was not tender. In the middle of the left shin was an area 4 in. long of moderate edema, slight redness and considerable tenderness. This area extended inward so as to include the middle third of the inner aspect of the lower leg. In this area, 1 in. to the right of the tibia, was a round, dark, brownish-red spot, 1 in. in diameter, slightly whitened at the center, very tender. The circumferences of the calves 3½ in. below the tubercles of the tibiae were, right 11 in., left 12½ in.

**Progress of case.**—A few hours after admission the patient's rectal temperature was 104.4°, his pulse 108, and his respirations 32. His hemoglobin by the Talqvist scale was 90%. His leucocyte count was 8,000. He became more delirious and tried to get out of bed. He was talkative, affable and mentally stimulated. He lived about fourteen hours after entrance, and during that time his rectal temperature rose steadily to 107.5°, his pulse rate to 180, and his respirations to 52. His pulse grew progressively weaker and was not palpable at the wrist for four hours before death. Almost up to his very death, long after his forearms and lower legs were pulseless, blue and cold, the patient's mind was alert, his eyes bright, and his face smiling, and he was talkative and delirious.

A blood culture was taken immediately after death. The blood was withdrawn from a vein under unfavorable circumstances. Both streptococci and staphylococci developed in the culture.

**Autopsy.**—The autopsy was performed by Dr. Oscar Richardson, seven and three-fourths hours post-mortem.

The meninges, vessels of Willis, sinuses, middle ears and brain were not remarkable.

The skin presented many small and large areas of purplish-red discoloration. The lesions described in the physical examination at entrance were but little changed except that they were purplish and some were larger. Section into the lesion in the vicinity of the right knee showed that the deep tissues were infiltrated with sero-sanguineous, gelatinous-like fluid. The muscle tissue in this situation was dark, sloppy and looked as if it were somewhat necrotic. On opening the right knee-joint much sero-sanguineous gelatinous-like fluid escaped. A cover-glass smear taken from this fluid showed on microscopical examination many streptococci. Section into the lesion of the left lower leg showed a condition similar to that in the tissues in the region of the right knee. Section of the tibia showed nothing remarkable in the bone or in the marrow.

Subcutaneous fat moderate in amount. Muscles not remarkable.

Peritoneal cavity free from fluid. Peritoneum, appendix, position of liver, diaphragm, not remarkable.

Pleural cavities free from fluid. The lungs were bound down everywhere by old membranous fibrous adhesions. The bronchial lymphatic glands, the tongue and the larynx were not remarkable. The trachea and bronchi contained a moderate amount of bloody, mucus-like material. In the upper part of the upper lobe of the right lung there was a fibrous, indurated mass about 5 cm. in each dimension. The mass showed, scattered through it, smaller and larger fibro-calcareous masses. The apex of the left lung showed a similar mass. The lungs elsewhere showed no

areas of consolidation, but they were infiltrated with considerable blood-like material.

Pericardium not remarkable. Heart weighed 240 gm. The heart was rather small. On section the myocardium was firm and slightly pale and cloudy. The valves and cavities were not remarkable. The foramen ovale presented an oval opening about 1 cm. in its greatest dimension. Coronary arteries free and smooth. The aorta showed a smooth intima with areas of purplish staining.

The liver weighed 1,530 gm. On section the tissue was firm, rather homogeneous and of pale, brownish-yellow color. No stones in gall bladder. Bile ducts free. Pancreas and duct of Wirsung not remarkable. The spleen weighed 135 gm. and was purplish and mushy. Adrenals not remarkable.

The right kidney weighed 114 gm. The capsule was stripped easily, leaving a pale surface with areas of depression. On section the pelvis showed moderate dilatation. Several of the calices were considerably dilated, and the calices generally showed moderate dilatation. About the calices which were most dilated there was considerable atrophy of the kidney tissue. In places only a narrow layer of the cortical portion of the kidney remained. The small areas of depression noted above were over the atrophied portions of the kidney. The markings of the kidney were plain. The section surfaces were somewhat purplish and cloudy. The pelvis contained a moderate amount of thin cloudy fluid. The first portion of the right ureter was slightly dilated, and at a point about 3 cm. from the pelvis, this ureter was completely occluded by an ovoid stone, measuring about 1.5 cm. in greatest dimension. The left kidney was not remarkable except for the section being purplish and cloudy.

Bladder, prostate, seminal vesicles and testes on section were not remarkable. In the situation of the urinary meatus there was a deep crevice-like depression which ended blindly and had no communication with the urethra. The urethra opened in the skin a little below this crevice.

Esophagus, stomach and intestines presented no lesions.

Cultures on blood-serum culture medium from the heart's blood, the spleen, the tissues of the right knee, and from the right knee joint showed profuse growth of the streptococcus pyogenes.

*Anatomical diagnosis.*—Septicemia (streptococcus), phlegmon of left leg, right knee and right hand. Soft spleen. Stone in the right ureter with occlusion of ureter. Hydronephrosis of the right kidney, chronic pleuritis, obsolete tuberculosis of the lungs, hemorrhagic edema of the lungs. Defective closure of the foramen ovale. Hypospadias.

The above report of the autopsy has been condensed from Dr. Richardson's record.

**CASE II.** A little girl, one and one-half years old, was brought into the accident room of the Massachusetts General Hospital on the evening of Jan. 27, 1908, and was admitted to the wards of Dr. Fitz. The parents were Russian Jews. The child was born in Boston.

*Family history:* Father, mother and sister well. No history of tuberculosis.

*Past history:* Child had been well and plump since birth. She ate, slept and moved her bowels normally. She seemed perfectly well up to day of entrance.

*Present illness:* In the early morning she felt cold and shivered and later seemed feverish. She was fussy during the day, and she vomited once in the afternoon. Her bowels moved twice during the day and the stools were loose and somewhat green and slimy. No cough or coryza or convulsions.

*Physical examination:* A plump, well-developed

child. Skin and mucous membranes of good color. Child lay on accident-room table with head slightly retracted and back straight. Temperature by rectum was 103.5°, pulse 180, respirations 44. Anterior fontanelle was about 1 in. in diagonal diameter, not bulging. Pupils equal and react to light. Movements of eyes normal, except for an occasional quiver of the eyeballs. Nostrils showed a few dry crusts. Alae nasi moved with respiration. Four teeth, two upper and two lower. Tongue was bright red and clean at the tip, coated in the posterior part. The throat was bright red, otherwise normal.

Heart not enlarged. Sounds regular, rapid, of good quality, no murmurs. Pulses synchronous, equal, regular, of good volume and tension.

Lungs were normal.

Abdomen was normal in appearance, soft, tympanitic. There were no masses or tenderness. The liver dullness extended from the sixth rib to  $\frac{1}{2}$  in. below the costal margin, where the edge was indistinctly felt. The splenic dullness measured  $1\frac{1}{2}$  by  $1\frac{1}{2}$  in., and the edge was not palpable.

The knee-jerks and plantar reflexes were normal. Kernig's sign was absent. No edema. No enlargement of lymphatic glands was made out. There was slight redness and roughening of the skin over the buttocks and thighs. There were many small excoriated papules on the skin of the body and limbs, including the soles of the feet.

A stool passed during the physical examination was small, soft, greenish-white, and contained considerable mucus.

The child cried when her head was brought forward into line with her body. Pressure on the back of her neck caused spasmodic movements of her legs and made her cry out as if in pain. Occasionally the child made a spasmodic movement of its body. The child was conscious, but she paid little attention to her surroundings.

During the examination the child had a severe convulsion, lasting about three minutes. The whole body became rigid, the eyes were turned to the left, and there were spasmodic movements of the arms and legs. The breathing was noisy and the child was cyanotic.

*Progress of the case:* After admission the child had no more convulsions. Her bowels were cleared and her stools became yellow, with little mucus. Nevertheless, the child grew progressively worse. On the day after entrance her neck was flaccid and not retracted, and it remained so. The child frequently held its arms rigid, sometimes with its elbows, wrists and fingers flexed. At times her breathing or crying was stridulous, suggesting stenosis of the trachea or larynx. The thymus dullness measured  $1\frac{1}{2}$  by  $1\frac{1}{2}$  in. Dr. A. Coolidge, Jr., saw the case in consultation and reported that the pharynx and larynx were reddened and that otherwise there was nothing definite found in the throat or larynx. Dr. H. L. Morse reported on the condition of the ears as follows: "Ears negative as a cause for temperature. Membrani both pink. Left one pricked. No fluid obtained." Culture from the throat was negative for the diphtheria bacillus and showed streptococci and staphylococci as predominating organisms. Lumbar puncture done on the day of her death showed a clear fluid with a few shreds, no cellular elements, no bacteria, negative culture.

The temperature rose irregularly to 106.5° and fell to 104° on the day of her death, the sixth day of the disease. The pulse rose to 205 and the respirations fluctuated between 40 and 60. On the day of death the pupils became unequal, a conjunctivitis appeared in the right eye, and the spleen was made out to be

enlarged to percussion. The child seemed blind and deaf, but was annoyed when moved. No stiffness of neck.

Immediately after death a blood-culture was taken, the blood being withdrawn from the heart with a long needle. Autopsy was refused.

The blood culture showed an abundant growth in pure culture of the streptococcus pyogenes.

The occurrence of these two cases in Dr. Fitz's wards in the same month raised the question whether streptococcus septicemia without discoverable point of entry and without preceding severe disease was not much more common than generally supposed. Search through the records of one thousand autopsies done in the Massachusetts General Hospital between Oct. 19, 1896, and Jan. 13, 1903, revealed no such case. In about one tenth of the cases cultures were not taken from the heart's blood. Streptococci were found in the heart's blood in 76 cases; in pure culture in 62 cases, and accompanied by other organisms in 14 cases. Not one of these cases was free either from some evident point of entry for the infection, as a wound, ulcer or abscess, or else from some severe and, in most cases, chronic disease for which the septicemia was terminal. Among the 62 cases which gave pure cultures 41, or about two thirds, had suppurating foci or wounds to explain the infection, and in the remaining 21 the infection was terminal to some severe disease. Of the 14 cases of mixed infection all but one showed a suppurating point or a wound. Thus it appears that a streptococcus blood infection is usually uncomplicated by the presence of other organisms when the infection is through some unknown portal and that, on the other hand, when there is a wide gateway such as an open wound or an abscess, more than one variety of bacterium are apt to enter.

In each of the cases reported a healthy person was taken sick and died of profound toxemia within eight days from the onset. One case showed the beginning local suppuration of pyemia, but the abscess stage was not reached. In both cases clinical observation, and, in one, autopsy failed to reveal the source of infection. Both patients had inflamed throats which may have been the place of entrance, but it seems plausible that the throat affection was secondary.

Although the infection of the blood with streptococcus is rare except as a complication, the differential diagnosis in obscure cases of severe infection is incomplete without consideration of streptococcus septicemia.

## THE ORIGIN OF URINARY CASTS; AN EXPERIMENTAL STUDY.

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It has been demonstrated by a good many experimenters that kidney lesions simulating very closely nephritis in man may be produced in animals by the injection of various irritants. Only

a few of these investigators, however, have given any account of the urinary findings, with special reference to casts, or of the origin of casts from the diseased kidney. Wallerstein<sup>1</sup> reports from studies of experimental nephritis in rabbits that urinary casts arise from epithelial cells, and that hyaline casts are an end result in the process of cell necrosis and degeneration.<sup>2</sup> The experiments here reported were undertaken at the suggestion of Dr. Henry A. Christian and were carried out in the division of the laboratory of the Department of the Theory and Practice of Physic, which is under his direction. The work was done in the hope of throwing further light on the question of cast formation.

The irritants used for producing nephritis were the same as those employed by previous experimenters for this purpose, with the addition of trypan red. All were given subcutaneously. Uranium nitrate was the first substance used, and it proved the most satisfactory. It was given in doses varying from one to five milligrams, but preferably in repeated doses of one milligram rather than in a single larger dose, since some of the animals were unable to survive one dose of one milligram. Potassium bichromate was given in doses of one half to one cubic centimeter of a 5% solution. Trypan red was used in saturated aqueous solution in doses of from one to five cubic centimeters. Arsenic was administered as Fowler's solution, in one to five minim doses. The last drug employed was cantharidin, given in doses of one milligram of a 1 to 2,000 solution.

Rabbits were used in all the experiments. They were kept in cages having an inclined bottom leading to a center, and by a tube into a bottle, so that all the urine was collected. Urinalysis was done daily, but only the excretion of albumin and casts was studied with any degree of thoroughness. It was often found difficult, in fact impossible in some cases, to get the urine perfectly clear. The presence of large numbers of bacteria, whose growth is favored by the alkaline urine, together with the precipitates of carbonates and phosphates, is largely responsible for this turbidity. Antiseptics were put into the collecting vessels with the hope of inhibiting the growth of bacteria, but the result was not gratifying. If a strong acid is added to the urine to neutralize it, such a violent reaction occurs with the liberation of CO<sub>2</sub> as to destroy the casts and interfere with filtration. The turbidity was most satisfactorily overcome by adding to the urine to be centrifuged a small amount of very dilute acetic acid solution. This is not strong enough to cause the liberation of CO<sub>2</sub> and yet helps very much in the examination of the sediment. To get the urine clear for determining albumin, the same dilute acetic acid was used and the urine filtered several times if necessary. Care must be taken not to add too much acid, a drop or two in a half wine-glass of urine is usually sufficient, for the urine becomes turbid again with an excess of acid.

<sup>1</sup> Zeitschr. für klin. Med., 1906, lviij 296.

<sup>2</sup> For the recent literature on experimental nephritis, see Christian: Theory and Practice of Medicine, BOSTON MED. AND SURG. JOUR., 1908, clviii, 416.