CHLOROMA WITH SPECIAL REFERENCE TO EAR,
NOSE AND THROAT MANIFESTATIONS, WITH
REPORT OF TWO CASES.

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Chloroma is a rapidly growing and very destructive new growth usually occurring in the young. It arises from the mother cells of the white corpuscles and is characterized, anatomically, by the formation of tumor masses, some or all of which have a greenish color. These have a predilection for bone and are most frequently found in or on the bones of the skull, but other tissues are also invaded. Usually the tumor cells are found in large numbers in the blood. Histologically chloroma may be divided into the myeloid or lymphatic types, according to the kind of leucocytes present. Clinically the condition most frequently manifests itself by tumor formations in the orbital or temporal regions, by swelling of the face with exophthalmos, tenderness over the affected bones, impairment of nerves due to pressure, a rapidly increasing anemia and cachexia with fever and an hemorrhagic diathesis.

The first description of this disease was by Allan-Burns¹ in 1821, while King² in 1853 was the first to name it chloroma. Since then about 100 case reports have appeared in the literature. Many of these are accompanied by most painstaking autopsy reports and pathologic discussions.

It was my good fortune to be present at the autopsy in 1892 of the first case reported by Dock and Warthin.³ It so impressed me that when I saw my first case the possibility of its being chloroma occurred to me. (It was not, however, until the clinical examination by Dr. Walter L. Bierring that the diagnosis was made. I was called in council because of the orbital condition and ear complications.)

A second case was referred to me and admitted to the Iowa Lutheran Hospital, March 18, 1919, with a diagnosis of orbital abscess. Having recently seen the other case and

failing to discover an origin for an orbital abscess, I immediately secured the results of successive blood examinations and became convinced that I was dealing with another case of chloroma. The subsequent history of the case, with death within a few weeks, was also in keeping with the diagnosis. Unfortunately I was defeated in my efforts to secure an autopsy.

It occurred to me that it would be of interest to this society to report the two cases which came under my observation, and to present excerpts from the recorded cases of chloroma which suffered involvement of the ear, nose and throat. (The autopsy findings in my first case with the chloromatous masses in the nasal sinuses, middle ears and right mastoid prompted this consideration.)

Case 1.—S. C., white boy, aged 12, entered the Iowa Methodist Hospital December 31, 1918.

Present complaint: The patient came to the hospital complaining of pain in the right ear and at the base of the brain. He is unable to close his right eye or to move the right side of his face. He further complains of hearing poorly on both sides, and states that he cannot see as well as he did a few weeks ago. He has pain in the right eye and in the lumbar region of his back.

His present illness began two weeks after he had recovered from an attack of influenza which went through the family in the early part of November, this year. He first noticed a "ticking" sensation in the left ear, and then a "thundering" in the right. Soon after this his right ear became painful. During the first week in December the patient observed that his right eye was black and that the eyeball was bulging. A few days later he noticed a bloody discharge from his nose. This lasted for a couple of days. During the time of the discharge his eye felt better. The pain in the right ear has been continuous, and his eyes have become more and more prominent. All of his symptoms have gradually increased.

Past history: He had infantile paralysis at the age of two. All extremities were involved, but he regained the use of all but the left foot, which remained partially paralyzed. Two and one-half years ago the right foot also became partially

paralyzed, and since that time he has never been as vigorous as other boys. But he has continued his school work. His appetite is good; he sleeps well. But since his entrance into the hospital his bladder has had to be catheterized. His father states that he was a full term baby and has been an average child in every respect. Family history negative.

Physical examination (W. L. Bierring): The boy is somewhat emaciated. The skin is pale and has a light yellow tinge. He is rather restless in bed. He cannot hear the ordinary voice, but when one speaks moderately loudly he understands questions and replies quickly and intelligently.

Head: The head is well formed. There is a moderate growth of hair. The base of the skull and the back of the neck are moderately tender to pressure. There is also tenderness over both mastoids. This tenderness is slightly more marked on the right side. Both eyeballs protrude markedly—the right more than the left. The right lids are somewhat swollen, purplish in color, and the venules of the lids on both sides are prominent. He cannot close the right eye completely. The right pupil is moderately dilated. The left pupil is normal, and both react to light and accommodation. There is marked engorgement of the lateral conjunctival vessels of the right eye. Nystagmus is absent. The eye movements are limited. He cannot read as well with the right as with the left eye.

There is moderate discharge from both ears. The nose is negative. The teeth are in fair condition. The tonsils are of moderate size. The tongue when protruded points to the right. The patient cannot wrinkle the right side of his forehead nor retract the mouth to the right. The superficial veins of the neck are distended. A few hard lymph nodes can be felt in each anterior cervical region. There is a moderate rigidity of the neck.

Thorax: The lower one-half of the sternum is somewhat depressed. The costochondral junction on the left side between the third and fourth ribs is slightly prominent. There is tenderness to moderate pressure over the upper one-half of the sternum. The lungs show nothing abnormal. There is a slight systolic murmur heard best at the base, but also

at the apex. Nothing abnormal can be detected by abdominal examination. The feet are in the position of talipes equinovarus. The reflexes of the upper extremities are normal. The patellar are absent, so are the Achilles. The Babinski sign is absent, but there is a suggestion of a positive Kernig on both sides.

Special examination: This examination, made December 31, 1918, showed marked congestion in both the middle ears. The right ear bulges. The hearing is decreased, a watch can be heard one inch away on the left side, and on contact on the right side. Paracentesis of the right ear drum was made and resulted in a small amount of a heavy discharge. Later this discharge became more fluid. The patient complained of pain over the right mastoid, which was sensitive to pressure. This continued throughout the illness. Radiograms taken on several successive days revealed a cloudiness of both mastoids, more marked on the right.

Eyes: The veins of both retinae are moderately congested. Before the fatal termination multiple hemorrhages appeared in both retinae. A marked exophthalmos was present in both eyes, more marked on the right side. A double optic neuritis was also present.

The patient continued to go downhill and died on the last of January. At the entrance there were 2,800,000 red cells and 24,000 whites, with hemoglobin, 45 per cent. On the 13th of January the white count reached 41,000. The day prior to death it was 18,000 with hemoglobin 20 per cent. In the differential count a rather large mononuclear cell, resembling myelocytes, predominated. This type of cell comprised between 90 and 100 per cent of all those found in the blood toward the last. While in the hospital the boy ran a continuous fever, which reached 104 two days before his death. He also developed a cystitis and had to be catheterized. An occasional granular and hyaline cast was found several times.

Autopsy report (Julius S. Weingart, M. D.): The body is that of a white male child, 57 inches in length. It is markedly emaciated. A mottled purpuric rash covers the abdomen and the lower part of the chest. A few purpuric blotches are present on the arms and on the lateral sur-

faces of the thighs. A bilateral talipes equinovarus is present, and also a dry purulent discharge from the right auditory canal.

Head: The dura in the cranial cavity is found adherent along the sagittal suture over an area 3 to 5 cm. in width and 8 to 10 cm. in length. It is also markedly thickened (in places to the extent of .5 cm.). This thickening is somewhat irregular and nodular in character. It is firm and thickest at the sinus itself, thinning out as it extends laterally. The color is greenish with scattered, dark, hemorrhagic areas. There is some engorgement of the cortical vessels in both right and left occipital regions of the brain. In the dura lining the left half of the posterior cranial fossa a mass about 2 cm. in diameter and 6 to 8 mm. in thickness, circular in shape, and slightly elevated above the surface of the dura, is seen. This has a distinctly greenish tinge. Examination of the venous sinuses shows nothing except that the wall of the right lateral sinus contains thickened areas similar in character to those seen about the superior longitudinal sinus. A small loose clot is found in the lumen. The interior of the right mastoid bone and the middle ear is filled with a gelatinous greenish mass. No definite pus is seen. Similar material also occurred in the sinuses of the sphenoid and in the right ethmoid cells. The brain itself shows nothing abnormal.

Thorax: A large flat greenish mass is seen on the posterior aspect of the sternum. This is of a greenish color, the most chloromatous of any of the tumor masses found. It is 5 to 6 cm. in width and .5 to 1 cm. in thickness, and extends from the manubrium sternum to the xiphoid cartilage. A similar flat greenish growth is found on the right vault of the diaphragm. The pleuræ and pericardium show a number of petechial hemorrhages. In the upper part of the lower lobe of the left lung there is an irregular area of partial consolidation. The heart and great muscles are normal. The mediastinal lymph nodes are not enlarged.

Abdomen: The gastrointestinal canal is negative. No definite enlargement of either mesenteric or retroperitoneal lymph nodes is present. The spleen is not enlarged. It weighs 7.5 ounces. The surface made by section has a reddish, waxy appearance. The liver is normal in size and weighs 3 pounds

3 ounces. The surface made by section appears normal, with the exception of some white striæ running along the blood vessels. Both kidneys are markedly enlarged, weighing 7 to 7.5 ounces and measuring 13 cm. by 6.5 cm. They are both white in color and mottled with hemorrhagic areas. The surface made by section shows a greenish cortex with numerous small hemorrhages in the pyramids. The bladder contains one ounce of purulent fluid. Its walls are extremely congested. Examination of the pancreas and adrenals is negative. The bone marrow from the center of the shaft of the femur is red and gelatinous. Microscopical examination of the wall of the longitudinal sinus shows the thickening to be due to a tumor mass composed of cells, round, or somewhat polygonal in shape, and arranged for the most part in strands between the fibers of the small amount of connective tissue which is present. These cells have nuclei, some of which are pyknotic, others have a loose chromatin network; the nuclei fill most of the cells, so that the amount of cytoplasm is very small. This latter is in many cases acidophilic. The cells are largely mononuclear, but here and there a cell with two nuclei or with a lobed one is seen. The size of the cells varies a good deal. No mitotic figures are found. Sections from the other tumors show precisely the same histologic picture: that of a cellular mass composed of strands and rows of mononuclear cells. The liver shows foci of similar character scattered throughout. Here in addition, a few very large multinuclear cells are seen which resemble closely the megakaryocytes of the marrow. The normal histologic aspect of the spleen is almost lost. The splenic bodies are very small. Often only a small group of lymphocytes can be seen here and there around the central artery. The rest of the spleen is packed with cells similar in type and arrangement to those seen in the tumor masses. Here very few red blood cells are seen. The marrow is replaced by the tumor cells. The kidney shows large areas where the tumor tissue has obliterated all the normal markings. In places the convoluted tubules and glomeruli are intact, but even here the tubular epithelium shows evidence of degeneration. Numerous areas of hemorrhages occur throughout the kidney substance.

Diagnosis: Myeloid chloroma.

Case 2.—R. B., male, aged 9, entered the Iowa Lutheran Hospital, March 18, 1919, with a possible diagnosis of orbital abscess. On account of my absence from the city, the patient was seen first by my assistant, Dr. Doane, who repeatedly examined the nose but failed to find any evidence of an infection. On March 24, Dr. J. T. Priestley was called in council. According to his report, the patient had been ill for several weeks, complaining of headache, general weakness, and aching of his limbs. More recently his vision had become somewhat disturbed. On examination the patient appears bright and takes a lively interest in things about him. Examination of the chest and abdomen reveal nothing abnormal. The long bones are all sensitive to pressure. The patient is unable to walk, but enjoys going about in a wheel chair. During his stay in the hospital the temperature varied between 99 and 102, pulse between 90 and 120, and respiration between 20 and 30. The urine was negative. The blood examination showed 2,000,000 red cells at entrance; before he left they dropped in number to 1,500,000. The whites were 33,000 at entrance, at one time reaching 56,000; 98 per cent of them were large mononuclear. Hemoglobin, 35 per cent; Wassermann negative. Radiogram of temporal bone showed nothing abnormal.

I examined the patient on March 29 and noted the following: The hearing is reduced on both sides. Examination of middle ear reveals nothing. There is a marked proptosis of the right eye, while the left is decidedly more prominent than normal. Both retinae show marked neuroretinitis. Pupils react to light and accommodation; the eye movements are but little restricted. Examination of the nose is negative. Before leaving the hospital, hemorrhage of the right retina occurred, and during his last days in the hospital several nasal hemorrhages took place; none were dangerous.

The boy remained in the hospital eighteen days, when he was taken home. He died about two weeks after.

Review of Literature.—Alexander⁴ states that he found lymphatic tumors in the labyrinth in leukemia, lymphosarcoma and chloroma.

Benjamin and Sluka⁵ mention the frequency of deafness and seventh nerve paralysis in chloromatous subjects. The

symptoms are due to the tumor deposits in the temporal bone.

Graupner⁶ relates the case history of a boy with a right-sided facial paralysis and vertigo. Both external canals were dropped and a slight discharge of fetid pus exuded from the right ear. The mastoid on this side was painful. Perception of the lower tones was lost. The patient ran a slight fever. The right mastoid was operated upon, and a green mass was found within. The facial canal was involved for a distance of one centimeter. The patient died nine days later, and among other chloromatous changes found was a tumor formation in the inner auditory canal exerting pressure on the seventh and eighth nerves.

Lehndorff⁷ prefaces the recital of two case histories of chloroma, stating that in many cases the usual clinical and blood picture is not present from the first. The two cases reported by him entered the hospital as septic diphtheria. The pharyngeal appearance, glandular enlargement, pulse, and temperature were those of diphtheria. One was a boy of 4½ years of age, who had been ill about fourteen days, suffering from a high fever, malaise and swelling of the submaxillary glands. Later he had a very foul breath, difficulty in swallowing, and frequent hemorrhages from the gums and skin and an increasing anemia. Examination revealed the left tonsil greatly swollen with a deep area about the size of that of a dollar covered with a foul gray green exudate that extended to the pharyngeal wall. At no time were diphtheritic bacilli found. There was a remission in the process and the temperature dropped to normal. The pharyngeal condition improved and apparently began to heal. A week later a short turn for the worse was noted, with high fever, increased anemia, and the tonsillar ulcerative process started anew, with increased glandular swelling in the neck. The child was removed from the hospital, but returned a few days later because of a developing dangerous pharyngeal stenosis. At this time the tonsils, palate and pharynx were covered with foul yellowish membrane. The enormous swelling interfered with speech, swallowing and breathing. After a few weeks' illness death ensued. An autopsy by Störk showed that the symptoms noted were due to chloroma.

Lehndorff's second case was that of a nine year old boy who began to suffer from malaise and fever in June. On June 12 he complained of sore throat. Diphtheritic antitoxin was injected on the 20th, and he entered the hospital with the diagnosis of septic diphtheria. The patient was emaciated and pale, with many old and recent subcutaneous hemorrhages. A high fever and rapid, poor pulse were present, and there was a systolic blowing heard all over the atria of the heart. The liver was soft and extended three fingers' breadth below the ribs. The spleen was relatively small, hard and palpable. The appearance of the throat suggested septic diphtheria. The breath was very foul; the tonsils were reddened and swollen; the uvula was swollen. On the left side there was a dirty, grayish yellow ulceration which extended over the left pillars. The exudate on the posterior pillars was thick, yellow and uneven. About the exudate there were hemorrhagic areas. These also occurred in the pharyngeal mucous membrane and on the cheeks. The glands under the jaw were small and painful, and the covering skin was edematous. Smears from the exudate showed diphtherialike bacilli, cocci in chains and clumps, fusiform bacilli and spirilla. The culture showed only staphylococci and streptococci. During the following days new hemorrhages appeared in the skin and mucous membrane, and the pharyngeal condition grew worse. The glands under the sternocleidomastoid were enlarged. The spleen and liver increased in size and grew softer. The following week the throat and pharyngeal condition remained stationary, but the temperature increased. The eye backgrounds were normal, and there was no exophthalmos. The bones were not painful. There was an occasional nasal bleeding. The axillary and inguinal glands were slightly enlarged during the last days of his life. The disease ran its course in about four weeks. The autopsy, performed by Weisner, showed beside other changes a chloromatous color in the glands of the neck and thorax. The histologic findings in this case were a surprise and indicated their importance in making the diagnosis.

Walls and Goldsmith⁸ reported a case of a five year old boy, whose illness covered a period of three months. The pathologic report showed chloromatous deposits in the fol-

lowing locations: orbits, frontal bones, nasal sinuses, temporal bone, external surfaces of the parietal bones, attached to the cerebral and spinal dura mater, kidney, liver and posterior surfaces of the sternum. One large chloromatous tumor was found between the eyes. This seemed to push apart the two halves of the face. The distance between the inner canthi was 3 cm. The pathologic findings in the larynx are of especial interest. "The upper part of the larynx shows necrosis as does also the epiglottis and fauces. The nasopharynx exhibits necrosis of the mucosa and submucosa and of some of the layers of striped muscle. Between the bundles of muscle fibers and even between the individual fibers are seen mononuclear cells, some of which are ordinary lymphocytes, but many of them are large cells supplied with large pale nuclei."

Hirschfeld⁹ reported the case of an eight year old girl who suffered from a growth beginning in the right antrum, of about six months' duration. When seen by him it exerted pressure outward and downward. The right alveolar process was lower than the left. The nose was crowded to the left. The seventh nerve was intact. The covering skin was cyanotic. The entire tumor was sensitive to pressure. An extension of the tumor up into the orbit and back of the eye produced a marked proptosis. The upper lid covered the eye but the lower one was ectropic. The eye was blind (the result of optic atrophy). The blood examination decided the diagnosis clinically as chloroma. Hirschfeld emphasizes the importance that the blood examination has in the presence of malignant tumors.

Merril and Bedell's¹⁰ case occurred in a boy of eight years with the following ear complications: The external canal of the right ear was moist and almost occluded with inspissated pus. The posterior superior wall was found bulging and moderately congested. The tympanic membrane showed a calcified area in the lower posterior quadrant. Above this was a small perforation through which a yellowish exudate escaped. The left ear showed a similar condition without the bulging posterior wall. Both mastoids were distinctly tender to pressure. No autopsy was permitted in this case, but a chloromatous tumor was uncovered in the left orbit under anesthesia a few days before death.

Bruce¹¹ reports the case of a married woman, aged 38 years, who suffered from violent neuralgic pains over the temporal region, cheek and upper jaw of the left side. She first noticed a swelling of the gum of the upper jaw in the region of the first bicuspid tooth of the left side. A day or two later she noticed a similar swelling at a corresponding point on the opposite side, and simultaneously a swelling made its appearance around the first bicuspid of the lower jaw on the left side. The pain subsided, but the swelling continued to increase. On examination, about six weeks from the onset, a marked swelling of the gums was seen. There were swellings under the jaw on both sides. The glands were fairly movable and not tender to touch. The other glands of the neck were not involved. The skin was swarthy. The breath was very foul. The teeth were all in line and not loose. The swelling of the gums was very marked, spreading between the teeth, and were convoluted, dark purplish red in color and covered with epithelium. They were firm to touch and did not bleed. The tonsils were not enlarged. Four days later there was an ulceration and sloughing over the first right molar above. A piece was removed for examination, and the pathologist reported that it was probably lymphosarcoma. About four weeks later the patient began to run a septic temperature from 100 to 104 degrees, with a pulse of 110 to 140. The swelling on the left side of the neck rapidly increased in size, as did also the growth on the gums. The breath was very offensive. There was much salivation and she was getting progressively worse. Pus was exuding from around the teeth and gums. It was thought that absorption of this pus was responsible for the temperature. An operation was undertaken with the object of not only removing the growth but of getting rid of the septic condition around the growth and teeth. She survived the operation only a few hours. The autopsy diagnosis was chloroma.

Pfeiffer's case¹² was that of a boy four years of age, who previously had fallen and cut the left side of his forehead, which healed promptly. Several weeks later he suffered with an inflammation of the other ear with a purulent discharge. Following this, the child continued ill with loss of appetite, and became pale. About two weeks later proptosis of the left

eye developed. A double papillitis with unequal pupils and limited motion of the eyes were noted. Examination of the left ear was negative, while a small perforation in the right upper posterior quadrant was present. Hearing on the right side was markedly reduced. The temporal and malar bones of both sides, and especially the left, were prominent. Proptosis of the right eye developed. A questionable diagnosis of tumor of the ethmoid or sphenoid and thrombosis of the cavernous sinus following the right middle ear infection was made and the skull opened external to the outer angle of the orbit and above the malar bone. No tumor or occlusion of the veins was found, although exploration with the finger reached the middle line and the region of the pyramid. The wound showed no tendency to heal. There developed a cerebral hernia, the bone margin became necrotic and death resulted after a four months' illness. At autopsy many yellowish green tumors, .5 cm. thick and about the size of a half dollar, were seen on the outer side of the dura. They were especially numerous along the wall of the longitudinal and transverse sinus. They were not attached to the bone. The entire right parietal bone and mastoid were found infiltrated with a yellowish green mass. The left tonsil, although not enlarged, showed the light greenish color. The submaxillary glands of both sides and collections about the larynx showed the same greenish deposits.

Saganuma¹³ reported a case in which both maxillary antri contained tumors.

Wynter and Laken¹⁴ report a case with the following autopsy findings: "The face is distorted. There is a considerable bulging of the cheeks due to immovable swellings in the superior maxillæ. Proptosis is present and the bridge of the nose is broadened and flattened. The skin below the eyes and upper portion of the face shows a greenish purple discoloration. Bleeding has evidently taken place from the gums and there are thickenings along the inner side of the lower jaw."

Pfeiffer discusses the clinical diagnosis of chloroma under four headings: First, there is painful exophthalmos with secondary optic atrophy. This is one of the earliest symptoms. Heyden found this to be the earliest symptom in 31 out

of 42 cases. In about one-fourth of the cases of chloroma the growth has its origin outside of the skull. Hence, exophthalmos is absent only in those cases in which the bones of the skull are not involved in the process.

The second series of symptoms are due to the growth of the chloroma in the temporal bone, causing middle ear infections, hemorrhages, tinnitus, reduced hearing and swelling and painful mastoids. These symptoms were present 25 times in the series of 42 cases. They are bilateral. According to Körner, chloroma is relatively more often met with in the external canal than any other tumor involving the ear. Disturbance of equilibrium resulting from chloromatous involvement of the static portion of the internal ear has been noted by Körner, Weinberger and others. Impaired function of the seventh nerve due to chloromatous infiltration has been repeatedly observed. Along with the ear disturbances there frequently appear chloromatous deposits under the temporal muscles, on one or both sides. Similar growths frequently occur in the nose, giving rise to hemorrhages which are sometimes fatal. In cases where the nose has been obstructed autopsies have revealed chloromatous growths in the sphenoid, ethmoid, antrum or pharyngeal vault (according to Körner, Chiari, Behring and Rosenblath). Strange to say, intracranial pressure symptoms, slowing of the pulse, vomiting, etc., have never been recorded, although growths along the venous sinus in the dura have frequently been present.

Thirdly, there is marked anemia, especially in the latter half of the disease. Many times the picture is that of a typical acute leukemia with an enormous increase in the number of white blood cells. The leukemia may appear suddenly shortly before death. (Rosenblath and Weinberger.) Coincident with this appear many large and small glands along the neck, mediastinum and abdomen. They are made up of one or more green nodules. Many times the spleen becomes swollen so that a diagnosis of leukemia is made.

The fourth point in diagnosis is the age at which the disease appears. Among 33 cases of chloroma, 28 appeared between the ages of one and twenty-five. Five cases were between the first and fourth years, eight between six and ten years. In cases of advanced age the growths are seldom found on the

skull. The number of male sufferers is greatly in excess of the females.

The disease usually runs a short course. Death ensues in the great majority of cases within three to four months. The direct cause of death is hemorrhage or general marasmus.

In conclusion, I believe it is important for the specialists in head work to be familiar with this condition in order that unnecessary operations may be avoided.

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