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SERIOUS COMPLICATIONS IN THE PUNCTURE OF
THE MAXILLARY ANTRUM. INVESTIGATIONS,
BY EXPERIMENTS ON ANIMALS, OF THE
REFLEXES PRODUCED FROM THE MU-
COUS MEMBRANE OF THE AN-
TRUM. AIR EMBOLI AFTER
ANTRUM PUNCTURE.

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It is a well known fact that occasionally, though fortunately seldom, puncture of the maxillary antrum may be attended with surprising and alarming phenomena in the form of long attacks of unconsciousness, often accompanied by convulsions. In the special literature available to me, I have found only nine fairly satisfactorily described cases, where the phenomena

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in question have been observed. Boenninghaus may, however, be right in saying that alarming symptoms after antrum puncture occur more frequently than is generally known. In my own practice and that of some of my colleagues no less than seven cases have been met with, a fact that seems to indicate that these dangerous complications are less uncommon than might be supposed, judging from the literature on the subject.

And even if these phenomena occur seldom, a great deal of attention should be paid to them as no less than the patient's life or health is at stake. In the nine cases found in the literature death supervened four times and in the seven cases collected by me, twice. There are evidently very good reasons for examining the various factors that may have brought about this result, especially as, to my knowledge, no satisfactory explanation of the mystical antrum exists. In this connection it may therefore be of interest to give a survey of the cases already published and of those met with in my own practice. The best known cases in the literature on the subject are probably the four mentioned by Claus.

1. A young girl of 19 had twice in the course of five years been treated for a left-sided maxillary inflammation. On both occasions a fairly large opening was made into the antrum through the lower meatus. Two years after the second treatment there was another recurrence of her antrum empyema. By that time there remained only a small fistula barely large enough for the passage of a probe through the previous opening in the lateral wall. A new puncture was therefore made with the commonly used Lichtwitz needle. It then appeared that the bone was so greatly thickened that the needle could hardly be made to penetrate it. An entrance into the antrum was however, successfully effected, and the air could be heard passing into the nose when the syringe was used. Suddenly the air met with considerable resistance, so that more than ordinary force had to be employed in order to compress the bulb. At the same moment the patient became cyanosed, with dyspnea and a feeling of fear, but with a strong, quiet pulse (75). She was immediately placed in a horizontal position and then quickly recovered, the cyanosis and dyspnea disappearing in the course of about ten minutes. There remained, how-

ever, a peculiar feeling of oppression for a couple of hours, but the next day she was as well as ever. The author supposes it to be a case of air embolism. The needle might possibly have been drawn backwards in the thick bone channel and the air driven into the cancellous portion of the bone.

2. A man, aged 68, suddenly lost consciousness after puncture of the antrum. On closer examination it appeared that the patient's right arm and leg were paralyzed, but not his face, and that he was unconscious and did not answer when addressed. Pulse strong and regular. On the following day the patient was clearer; he knew the doctor and could name various objects. His speech, however, was indistinct. He was able even then to move his right arm, and six days later no paralytic phenomena were apparent. Claus has here diagnosed cerebral apoplexy in the left hemisphere. He also does not consider it impossible that this has been a case of arterial spasm, a poisonous effect of the novocain adrenalin administered.

3. A young woman was treated with irrigation of the right maxillary antrum, and was twice syringed without unpleasant consequences. Immediately after a third syringing, cyanosis suddenly supervened, with loss of consciousness and an uncountable pulse, stertorous breathing and fixed pupil. Notwithstanding the administration of stimulants and artificial respiration, death occurred shortly. The anesthetic employed was six drops of a 10 per cent novocain solution with three drops of adrenalin in 20 minutes. The postmortem gave entirely negative results. According to Claus' view, the patient died of heart paralysis as a consequence of novocain poisoning.

4. A woman, aged 36, was anesthetized with a 10 per cent novocain suprarenin solution (1 per cent of an adrenalin solution 1/1,000) applied to the lower meatus on a tampon, and followed by painting 10 per cent cocain on a thin swab over the inferior turbinated bone and inferior meatus. Puncturing of the antrum was thereupon performed without difficulty with a Lichtwitz needle, and air was then injected into the antrum. At the same moment the patient lost consciousness, with suspended pulse and respiration. After camphor caffein injections and a saline infusion the pulse and respiration im-

proved; but consciousness did not return and the comatose condition passed into death.

At the postmortem examination there was found, among other things, a hemorrhagic infiltration, 5 centimeters in length and 2 centimeters in width, in the epicardium of the right ventricle. The infiltration could be traced right through the ventricular wall into the endocardium. A similar infiltration was also seen in the septum membranaceum. The heart, which was opened under water, contained no air. In the gray matter of the brain some slight hemorrhages were found. After opening the fourth ventricle, extravasations were also observable in the arbor vitæ and in the lower part of the cerebellum.

In this case, too, Claus considers that novocain poisoning was the cause of death.

Among other writers, Hajek, in his "Pathologie und Therapie der Nebenhöhlen der Nase," points out that long attacks of unconsciousness may now and then occur in connection with exploratory punctures. These must not be confounded with the slight fainting fits that are not infrequently seen during intranasal manipulations, due partly to the effect of the cocain and partly to the feeling of fear and the psychic shock which often attend the operations. The long attacks of unconsciousness "durch den Eingriff ausgelöste hystero-epileptische Anfälle," may last for hours, and are not infrequently associated with convulsions. Hajek has repeatedly observed, especially in patients with a narrow ostium maxillare and a bad outlet for the fluid, long periods of malaise with cold sweats and palpitations, and slow strained pulse (down to 60 as against 70 and 80 normally). The author considers these symptoms as the expression of a vagus irritation produced reflexly through irritation of the second branch of the trigeminal. Hajek once had a case of true apoplexy after antrum puncture, from which the patient, a diabetic, with arteriosclerosis, died within 24 hours.

Killian, in 1913, at a meeting of the German laryngologists at Stuttgart, described a case of sudden "antrum death" after syringing of the antrum. A postmortem, with special examination of this cavity, gave an entirely negative result. The only thing that could be definitely established, was that the syringed water had been cold. During the discussion that

followed, Streit (Königsberg) stated that after syringing through the middle nasal fossa, he had observed temporary paralysis of both legs, and temporary disturbance of vision. Siebenmann (Basel) considered the attacks of giddiness after irrigation of the antrum to be action of the vagus produced by trigeminal irritation.

Neuenborn treated a young man of 23 for double sided antrum empyema. On the left side puncture and syringing were twice performed without inconvenience of any kind. Two days after the second treatment the right antrum was punctured, with subsequent evacuation of pus and injection of air. Immediately after the removal of the canula, the patient fell from his chair, respiration ceased and the pupils were fixed and dilated to the maximum. His face was pale with cyanosed lips. His entire body was rigid and in a condition resembling that of tetanus, so that artificial respiration could not be proceeded with, owing to muscular spasms. The pulse was good and regular, 72. Massage of the diaphragm was performed until, after 25 minutes, spontaneous respiratory movements recommenced. These were at first irregular, with frequent interruptions, and the massage had therefore to be continued. After some time the condition of tonic spasms improved, but became worse again directly an arm or leg was moved. It was only after two hours that the spastic condition passed away; but it returned again later with tonic spasms alternating with clonic contractions. The pupils were still fixed and dilated to the maximum. During the three following days the patient was unconscious, but with normal pulse and temperature, except for one rise in the latter to 38.2 the day after the first attack. On the fourth day after the puncture, consciousness began to return. The patient then complained of headache and nerve pains with spots specially tender to pressure over the trigeminus and the ischiadicus.

The author maintains that this was a case of cocain poisoning. He recalls, in this connection, E. Falk's investigation of the toxic effects of cocain, according to which the respiration is first of all affected, and that consequently a death from cocain is due to a cessation of respiration. The above case, with good, strong pulse all the time, would therefore

answer particularly well to the characteristic picture of cocaine poisoning. Neuenborn does not, however, seem to be quite sure of the matter. He points out, for instance, that the cocaine solution ($7\frac{1}{2}$ per cent, of which about 0.1 gm. was soaked up into a thin wool swab for painting three times) was very weak, the patient moreover having repeatedly been anesthetized before with the same solution. The author therefore believes that something else may have supervened, which he cannot explain, but imagines must be sought in the actual syringing.

Henrici has also described two cases that are of considerable interest. In the one case, in which the patient suffered from empyema and formation of polypi, the polypi were removed under local anesthesia, with subsequent irrigation of the frontal and maxillary sinuses. While one of the antrums was being syringed the patient suddenly collapsed and had an epileptoid attack, with cyanosis and trismus. Respiration was labored, and the pulse weak and irregular. The pupils were fixed. The patient recovered quickly, however, apparently without unpleasant consequences. The following day the antrum was again syringed. The result was the same as before. The lockjaw this time was so severe that the mouth could not be opened with a gag. The chest was quite rigid as a probable consequence of the spasmodic contraction of the respiratory muscles. Even after tracheotomy it was impossible to carry out artificial respiration, and the patient died without regaining consciousness. A postmortem examination gave an entirely negative result.

In the second of Henrici's patients, too, nasal polypi were removed under cocaine. After 10 per cent cocaine applications to the middle meatus, the antrum was to be syringed through the middle nasal fossa. As soon as the syringing began, an epileptoid attack occurred also in this case, with labored respiration, cyanosed face, and clonic contractions in the arms and legs. The pulse was suspended. Under artificial respiration and heart massage, the patient grew rapidly better, but for a time both arms and legs were paraplegic. For a little time after the attack, she was not quite mentally clear. She was unable, for instance, to explain where she was. By degrees, however, all the phenomena disappeared; but for

two or three years after the treatment the patient felt a weariness in her arms and legs, and was forgetful and listless. Henrici draws attention to the fact that neither of his patients suffered from epilepsy or any other inherited ailment. He could not explain the cause of the attacks, nor whether it was cocain or some other factor that had contributed to their occurrence.

Zarniko gives an account, in his textbook, "*Die Krankheiten der Nase und des Nasenrachens*," of a woman of 50 who was subjected to a puncture of the antrum. The perforation was made through the lower nasal fossa, and the operation was performed with the greatest ease. When Zarniko proceeded, after injecting air, to rinse out the cavity, the patient suddenly collapsed with a sigh. Her face was pale, the skin cold and covered with perspiration. The pupils were fixed and dilated to the maximum, and the pulse and respiration were suspended. She was immediately placed upon the floor, and artificial respiration was begun. The patient's condition was very critical, and Zarniko even feared that death might occur at any moment. By means of artificial respiration and stimuli, however, the color was brought back after a time to the bloodless lips; a faint moaning respiration was heard, and the patient awoke to consciousness. In the course of an hour she was able to go home. The author considers this collapse to have been only a result of trigeminal irritation. The patient was not weak or apprehensive, and had had cocain several times before without any poison effect having been observed.

From these cases it will be seen that the literature on the subject contains only scanty information regarding bad results after puncture of the antrum. A continued search might possibly bring others to light, but it is not likely that their number would be very great. The literature does not, however, give an entirely correct representation of the matter as it appears in practice. These tragic cases, indeed, are rare, but scarcely as rare as our literature on the subject would make it appear.

In addition to the cases mentioned above, I shall describe four that have occurred in my own practice.

1. A man of 51 had been for some considerable time under treatment for double sided acute antrum empyema. On the left side the antrum, after local anesthesia with 10 and 20 per cent cocain solution, was punctured and then syringed several times through the artificial aperture without causing any inconvenience to the patient. As the secretion on the right side, in spite of conservative treatment, continued undiminished for a considerable period, an opening was to be made here too into the antrum. An exploratory perforation was first made with the ordinary Lichtwitz needle through the lower meatus. The bony wall on the right side, like that on the left, was hard and thick. After it had been perforated, air was as usual first introduced in order to find out whether the ostium maxillare was permeable. It then appeared that the air injected met with considerable resistance. At the same time a peculiar bubbling sound was heard inside the antrum, and suddenly the patient sank down unconscious, his face becoming cyanosed. Respiration had ceased instantaneously in the inspiratory position. The jaws were firmly pressed together, and the whole body was rigid, as if the muscles of both the trunk and the extremities were in a condition of general tetanic contraction. The pupils were not especially dilated, but were completely fixed. The pulse, which at first could not be counted, was later felt to be rapid, irregular and small. How long this condition of absolute cessation of respiration lasted cannot exactly be said. A wedge was quickly, though with considerable difficulty, pushed in between the teeth, and the tongue drawn forward, whereupon a few irregular stertorous respirations occurred. The convulsive rigidity of the extremities at the same time gave place to clonic contractions in the upper and lower extremities. As soon as possible, after camphor caffen injections, artificial respiration was begun and carried on without much difficulty after the tonic spasms had ceased. The patient's condition now gradually improved. The irregular, stertorous breathing ceased and the cyanosis disappeared. After about 20 minutes consciousness returned. The patient was immediately put to bed, and by the next day was well enough to be discharged. For several weeks, however, he felt tired and without interest in his work.

According to his own statement, the patient had always been strong and well, and in his own opinion bore physical exertion without difficulty. He did not give one the impression, however, of being a strong man, but on the contrary looked delicate. It was subsequently stated by his relatives that 30 years previously he had had two epileptic fits, but as far as they knew there had been no recurrence of them. There was, moreover, epilepsy in his family, two brothers who died at the age of 35 having suffered much from that disease. There was nothing remarkable about the heart and lungs. The urine showed normal conditions. Has since been repeatedly examined by internists with negative results.

2. A man of 54 had been treated for acute left sided influenza otitis with paracentesis. On account of constant violent pain in the left half of the face and in the teeth on the same side, a puncture of the maxillary sinus was performed in order to ascertain whether inflammation of that cavity was the cause of the pain. The perforation of the bone, which was performed under cocain, with a 10 and 20 per cent solution, required the exercise of considerable force, as the bone in the lower meatus was thick and hard, so that the trocar only penetrated by slow degrees. During the injection of air, a bubbling sound was heard and interpreted as a collection of fluid in the cavity. In this patient, too, the air appeared to meet with more resistance than usual, though not greater than may often be experienced when the ostium maxillare is narrow. It was therefore thought that syringing could be carried out without risk. Just as the syringe was being transferred, however, after the injection of air, to the water vessel, the patient dropped from his chair under circumstances resembling those just described in the case of the first patient, with cyanosis, absolute cessation of respiration, fixed pupils not greatly dilated, uncountable pulse. Both body and extremities were rigid, the entire muscular system being in a condition of general tetanic contraction. Notwithstanding the trismus that was present, we succeeded in opening the mouth and drawing the tongue forward, whereupon artificial respiration was begun. The continued respiratory spasm, however, at first occasioned very great difficulty; but after a time, it is not known how long, involuntary respiratory movements could be ob-

served, the first very shallow and irregular, but, with continued artificial respiration, becoming constantly deeper. After camphor caffein injections, the pulse could once more be felt. It was feeble, irregular and rapid, 100 to 120. After from 15 to 20 minutes the corneal reflex returned, and after about 30 minutes the patient regained consciousness, though at first he was confused. He did not know, for instance, where he was; and it was not until half an hour later that his mind became sufficiently clear for him to understand his surroundings in a measure. In contrast to the first mentioned case, there were no convulsive movements. The muscles of both the trunk and the extremities appeared throughout the attack to be spastically contracted. After the attack, too, the condition of tetanic irritation continued in upper and lower extremities. Arms and legs were thus rigid, and could not be actively moved, and passively only with difficulty. At the same time the patient complained of a peculiar feeling of numbness, especially in hands and feet. His condition improved, however, rapidly. In the course of an hour he was once more able to move his arms and legs, though not without considerable difficulty. If he attempted, for instance, to raise his right or left hand to his mouth, he failed to do so, the hand moving out to the side. If he wanted to move his foot from one side to the other towards a certain point, the leg, indeed, could be carried over in the right direction, but the foot kicked out into the air when it was meant to touch the given point. The patellar reflex was lively, but did not appear to be increased to any great extent. The same evening, six hours after the trauma, the arms could be moved considerably better, but did not regain their full power until the next day. For a long time, however, the pressure of the left hand was weaker than that of the right. The patient had to remain in bed until the second day after the puncture. The right leg was then sufficiently well for him to be able, when supported, to limp across the room; but it was not until the fourth day after the attack that the left leg could be used with any feeling of security. The numbness, which was strongly marked in the left leg, especially during the first few days after the trauma, was also sufficient to necessitate the use of a stick during the six to eight weeks following.

Three years later the patient still complained of feeling a little numb in his left foot, especially in the second and third toes, so that he felt insecure when, for instance, he went up or down stairs. A thorough examination was then made by a nerve specialist, but no disturbance of sensation could be found.

It was considered that the idea of disease of an organic nature was on the whole precluded.

The patient was a slight, somewhat nervous and over-worked man, but was considered to be energetic and capable in his calling. Had further always had good health except when, during a very fatiguing visit to America, he had been rather subject to heart trouble. Had never had epilepsy nor was that disease in his family. Lues was denied, and Wassermann was negative. There was nothing remarkable about the heart, lungs and urine, either in this or in any subsequent examination by specialists for internal medicine. A skiagram of the maxillary antra showed both to be large and well developed.

2. In a farmer of 61, with symptoms of an empyema of the antrum of Highmore, the antra were about to be examined. After local anesthesia of the left lower meatus with a 20 per cent cocain solution, the perforation was performed quickly and easily in the ordinary way. The antrum contained numerous mucopurulent lumps. In manipulating the left antrum, a wool holder with 20 per cent cocain was introduced into the lower nasal fossa on the right side, after which the puncture on that side was performed without difficulty. While this was going on the patient was apparently well, but complained that the anesthesia was considerably less effectual than on the side first punctured. There was then no indication of the cocain intoxication. The pupils were not dilated, and the patient was talking all the time about his case and the troubles consequent on it. When the perforation on the right side had been effected, the injection of air was proceeded with. As the air at first passed through the antrum without resistance, several compressions of the bulb were made in rapid succession, and at last a mucopurulent mass was blown out through the maxillary ostium, which it blocked as it passed through. As a consequence of this the pressure rose in the

antrum and could be distinctly felt in the bulb, which required greater force to compress it than before, in order to remove the lump of secretion from the antrum. At that instant the patient fell prostrate, cyanosed and without respiration. Stimuli and artificial respiration for about half an hour produced no result. Death seemed to have been instantaneous.

There was no opportunity of making a postmortem examination. A wide opening was made, however, in the canine fossa. The antrum was found to be very large and the punctured opening in the usual place, apparently without having detached the surrounding mucous membrane.

The patient was said to have always been a strong, healthy man, one of those mountain dwellers who can bear great physical exertion without ill effects. No further particulars were available.

4. A farmer of 62, with left sided antrum empyema of uncertain duration, was to undergo puncture of the maxillary antrum. This was done through the lower meatus quickly and easily after anesthetizing with a 20 per cent cocain solution. As the man had bronchitis, with sibilant breathing distributed over the dorsal surface, and was also pale and exhausted looking, he was placed, for safety's sake, on a couch before the injection of air was begun. The cocain did not appear to have caused him the slightest inconvenience; and notwithstanding careful observation, no indication of cocain poisoning could be discovered. No dilatation of the pupils. Without any difficulty whatever, the patient walked, with the needle inserted, into the adjoining room and sat down upon the couch. He felt at that time quite well. A careful injection of air immediately showed that the air met with considerable resistance. As soon as the pressure in the antrum was increased, the patient began to complain of difficulty in breathing. He could not get air, was cyanosed, and had a marked feeling of apprehension, cold sweat and uneasiness. He was immediately placed in a horizontal position, and the trocar was removed. Respiration was irregular and shallow, coming in groans, and the face was still cyanosed. The pulse was small, hardly perceptible. In the course of ten minutes the respiratory movements became once more deep and regular, the cyanosis disappeared, and the patient felt

better. Half an hour later he was quite well again, and was able to leave the consulting room without assistance.

This case greatly resembles Claus' case No. 1, where similar symptoms appeared without, however, being followed by serious complications.

In addition to the above four cases, I have collected, in chance conversations with colleagues, three more cases, which I am kindly permitted to describe.

1. Reported by recollection by Dr. Fleischer, Kristiania.

In a young, apparently healthy woman, antrum puncture was to be performed. The needle was introduced through the lower meatus, where the bone was thick and difficult to penetrate. The puncture was performed, however, as usual. During the air injection that followed, the patient sank down unconscious, with stertorous, irregular breathing. The comatose condition continued until death supervened twelve hours later. The postmortem gave no definite explanation.

2. Reported by Professor G. Holmgren, Stockholm.

A woman of 65 was treated for a chronic maxillary sinusitis with slightly fetid secretion. Syringing was performed on several occasions, when, on account of the narrow space and of the patient's sensitiveness, a Lichtwitz needle was employed through the lower meatus. After the introduction of the needle, and before the syringing, air was injected. Immediately after this the patient became deathly pale and pulseless and collapsed. At the same time a peculiar gurgling sound was heard, as of tiny air bubbles. They gave an impression of moving quickly down along the jugular vein. The patient was much exhausted for many hours, but grew better later; and on the next day she had recovered without any ill effects worth mentioning.

3. Reported by Dr. Roll-Hansen, Kristianssand.

The patient was a woman of 34, who, up to that time, had always been well with the one exception that for a rather long time she had been troubled with obstruction of the right half of the nose.

On examination, the right nasal cavity was found to be almost filled with polypi, which appeared to come from the anterior ethmoidal cells. After local anesthesia with cocaine (15 per cent), some of the cells were removed in the usual

way and without difficulty. The patient was quite well after the brief treatment. In order to ascertain whether there was also an antrum empyema, a puncture was made under cocaine anesthesia, with an ordinary straight cannula, in the usual place below the inferior turbinated bone. There was great difficulty in passing the cannula through the bone, on account of the hardness of the latter. As the needle pierced the bone the patient turned rather pale. The perforation was nevertheless completed, and then a careful injection of air was attempted. The air could not be heard to pass out through the ostium maxillare, but at the first pressure on the bulb of the syringe the patient suddenly fell to the floor as though struck by lightning, and lay there at full length, quite unconscious. There was complete rigidity of body and limbs, respiration was rapid and stertorous, and the pulse was also rapid, about 120 (average). The attack lasted five minutes, after which consciousness returned. Tonic rigidity of the trunk and extremities were found, but on the other hand no clonic movements. The color of the patient's face during the attack was paler than her normal, somewhat ruddy complexion. When consciousness returned, she was able, with the nurse's assistance, to walk into the adjoining room, where she was put to bed. For a time immediately after the trauma, the patient suffered from paresis of the right arm. About five hours after the puncture a fresh examination was made. Aphasia was then present. The patient could not find the right words and was unable to recollect even quite ordinary expressions. The pressure of the hand on the right side was rather weaker than on the left. After five days had passed, all the phenomena disappeared, and there was no longer any aphasia. She left the clinic without further trouble of any kind.

The cases that have now been mentioned may together form a very good foundation for a solution of the problems that in this connection present themselves. When we endeavor to ascertain the nature of the factors that have here cooperated we must in the first place keep in mind the fact that from a theoretical point of view the alarming symptoms may just as well have originated in what took place before the operation, namely, in the anesthetizing, as in the operation itself, with the subsequent injection of air and syringing. We will first

consider the cocainization and the part it may be supposed to have played in these cases.

COCAIN POISONING

and its symptomatology are discussed in detail, *inter alia*, in Paulsson's "Lehrbuch der Pharmakologie." The author emphasizes the fact that acute cocain intoxication presents a varying picture. The slighter cases appear as a feeling of languor, giddiness, fear, pallor and indications of syncope, or as excitement, talkativeness, hallucinations and delirium. In more serious cases there is also dilatation of the pupils, dryness of the mucous membranes, vomiting and clouded sensorium. The heart is always affected, with irregular pulse, now rapid, now slow, pale face and the tip of the nose cyanosed, occasional rises of temperature, finally collapse with cessation of circulation and respiration (Cheyne-Stokes). In addition clonic contractions or tetanus, after which death ensues as a consequence of heart and respiration paralysis. After injection of large quantities, e. g., one gramme, death may be instantaneous. It is difficult to say what the lethal dose is. Serious symptoms have been observed after only a few centigrammes, and little or no harm has resulted from a dose many times larger. It may therefore be assumed that individual disposition has something to do with the matter. Cocain in concentrated form is very much more dangerous than in weak solution, as in the first case a considerable portion of the poison is absorbed, while in the diluted form it is to a great extent confined to the place of application and rendered innocuous.

The toxicity of novocain is only from one-sixth to one-eighth that of cocain. Paulsson has experimented upon himself by injecting 0.4 and 0.75 gr. After the first dose no symptoms of poisoning appeared, and after the second only transitory symptoms.

It will from this be apparent that it is only the serious cases of cocain poisoning that can come under consideration in connection with our histories of cases. How large the dose must be to prove fatal in any particular case is not known; but we should at least be able *a priori* to take for granted either that the dose administered must have been

excessive as compared with that ordinarily used, or that these patients must have had an idiosyncrasy for cocain.

If we now consider the doses given, we find, as already mentioned, the following: For anesthesia sometimes novocain adrenalin, and sometimes cocain is employed. Novocain is used by Claus in a 10 per cent solution, of which 6 drops plus 3 drops of adrenalin are placed in the inferior meatus for 20 minutes. That these small doses should be capable of producing poisoning symptoms of the most serious nature is contrary to all our experience in the employment of novocain adrenalin in intranasal operations. By way of comparison it is only necessary to recall Paulsson's experiments, among which 0.4 gr. of novocain were even injected without the slightest effect of poison. Claus himself maintains that it must have been a novocain poisoning, but expresses, it is true, his astonishment that this should twice occur in this particular operation of puncturing and syringing the maxillary sinus, when otherwise, notwithstanding an extensive employment, both clinical and polyclinical, of novocain, he had never seen unpleasant consequences from this anesthetic. Neuenborn has used cocain in a $7\frac{1}{2}$ per cent solution, of which 0.1 gm. is taken up by a thin wool swab which would then contain 0.0075 gm. of cocain. It is stated that with this solution anesthesia is attained only after three applications of the swab. Neuenborn thinks that this minimal dose has produced cocain poisoning in his patients; but he does admit the possibility of the occurrence of a further factor, which he cannot explain, but which he thinks must be sought in the syringing itself.

In the discussion that took place in connection with Neuenborn's statements, it was maintained in many quarters that it could hardly have been cocain poisoning from the application of so weak a solution. Henrici, for instance, who, in the cases reported by him, had employed 10 per cent cocain in careful doses, is emphatic in his opinion that some other factor must have been active.

On my own patients I have used cocain in 10 and 20 per cent solutions. The anesthetization was performed in the following manner: An Uchermann's wool holder was firmly wound round with wool, and saturated first with 10 per cent, and in the final swabbings with 20 per cent cocain, which

was rubbed into the front part of the inferior meatus only at the place where the perforation was to be made. In order to prevent the cocain, when introduced into the narrow nasal passage, from being pressed out of the swab and running back into the nasopharynx, the swab is always squeezed out, and is thus never wet, but only damp. The last swabbings before the perforation is made, are, as I have said, with 20 per cent solution, as experience has convinced me that a solution of that concentration is necessary to obtain sufficient anesthesia, especially where the bone is thick, and where, moreover, there is inflammation in the antrum. Personally I consider even a 20 per cent cocain solution, employed in the above manner, to be quite safe. On all the thousands of occasions on which I have administered cocain, both when acting as assistant physician at our State Hospital and in my private practice, I have never once observed dangerous symptoms of poisoning after 20 per cent applications administered in this manner. Slight intoxications, such as languor, giddiness, etc., may of course have occurred; but these phenomena have always quickly disappeared when the patient has been placed in a horizontal position. To the best of my belief cocain solutions of 20 per cent strength have been used for a number of years in the State Hospital's Otolaryngologic Polyclinic in Christiania without serious consequences ever having been observed. Moreover in the cases in question only a relatively small part of mucous membrane was anesthetized. If a 10 to 20 per cent cocain solution, employed as indicated above, were attended with danger, it seems remarkable that the unpleasant consequences did not first of all appear in one of the intranasal operations, where the cocainized region was of far greater extent than the case here. It is possible that among the cases described in the literature on the subject there have been some individual instances of intolerance, although this explanation does not seem especially obvious, considering that most of the patients had been anesthetized several times before the fatal puncturing (Claus', Neuenborn's and Henrici's cases). Of my patients, No. 1 was treated with cocain adrenalin every other day for two or three weeks without the slightest ill effects. In the case of No. 2 a series of cocain administrations with a 20 per cent solution was subsequently given

for another nasal affection, without occasioning the slightest inconvenience to the patient.

A perusal of the history of the cases shows, moreover, that these attacks have not followed directly upon the anesthetizing. In none of my patients could any sign of poisoning be discovered after the cocainization. Nor does the little shock which so often accompanies the perforation of the antrum wall appear to have been of any importance; on the contrary, the patients stated, after the perforation, that they felt quite well. It was not until the injection of air or the syringing was performed that the alarming phenomena appeared. If it was an effect of cocain that here asserted itself, it is very remarkable that without any premonitory symptoms whatever, it should appear in apoplectic form, in immediate connection with the introduction of air or of water into the antrum.

There is on the whole so much here that speaks against the theory of cocain poisoning that it is impossible to feel entirely satisfied with this diagnosis. The anesthetization may be a predisposing factor, but scarcely the decisive one. There must be, as Henrici says, some other factor that is cooperative. We ought therefore first of all to see whether an explanation of these mysterious phenomena cannot be found in the operation itself and the consequent injection of air into, and syringing of, the antrum. We have here only two possibilities to consider. There must either be, as several writers have indicated, a reflex of an unknown nature from the mucous membrane of the antrum, or the operation must have produced an air embolus.

I will first mention the points that favor the former of these possibilities, the reflex theory. Before describing the investigations connected with it, it will be as well to give a general survey of the reflexes originating in the nasal mucous membrane itself.

THE NASAL REFLEX NEUROSES.

The nasal reflexes, or reflex neuroses, are well known and have been much discussed, particularly in the special literature of the eighties and nineties of the last century, while the antrum reflex still remains a *terra incognita*. As, however, the mucous membranes of the maxillary antrum and of the

nasal cavity are innervated by the same nerve trunks, it is obvious that all the reflexes from the mucous membranes of the nose and of the antrum should be viewed from the same visual angle and all treated alike as nasal reflex neuroses.

It has long been known among rhinologists that a number of diseases occurring especially in paroxysms have been affected by intranasal treatment of the pathologic changes in the mucous membrane of the nose. Voltolini was the first to emphasize the connection that there appears to be between various asthmatic conditions and nasal polypi. As the asthmatic attacks became less severe after the removal of the polypi, it was his opinion that the latter were the cause of the asthma, and he came to the conclusion that "either the polypi reflexly produced the asthma, or these new formations, in obstructing respiration, altered its chemical processes and thereby the structure of the lung tissue."

Voltolini's work, however, aroused no special attention. It was Fraenkel who first of all caused the nasal reflex neuroses to become a much discussed subject in the special literature of the eighties of the last century. Fraenkel, in his well written work, "Ueber die Zusammenhang von Asthma nervosa und Krankheiten der Nase," maintained that asthma with nasal polypi must be regarded as a reflex spasm localized in the bronchi muscles, called forth by an irritation of the sensory nasal nerves. In response to Fraenkel's work, contributions poured into the medical journals from all sides. At first the discussion had special reference to bronchial asthma and its relation to intranasal pathologic changes of various kinds. It was not long, however, before the field of nasal reflex neuroses was extended to other subjects. Hack and his pupils, among them Fliess, led the way. One group of diseases after another was said to have its origin in pathologic changes in the nasal mucous membrane—migraine, supra-orbital neuralgia, vasomotor disturbances of the vessels of the skin, epilepsy, amaurosis, articular rheumatism, Basedow's disease, diabètes, diseases of the heart and stomach, dysmenorrhea, etc., ad infinitum. Everything was due more or less to nasal reflex neuroses, which at last seem likely to become the inexhaustible source of all evil.

As a matter of course, all these articles on the subject of

healing diseases of the most varied character by galvanocautery or other intranasal treatment, made a great sensation, and criticism was not long in making itself heard. The exaggerations were sharply attacked, and the enthusiasts who had gone to extremes were unable, in the long run, to maintain their position. There was a great rebound, and skepticism even went so far as to deny altogether the existence of reflex neuroses. A detailed account of the numerous contributions of the eighties and nineties of the last century would here carry us too far, for they occupy too much space in the special literature. The contention about the nasal reflex neuroses has been of great importance from the fact that it has drawn attention to the by no means insignificant part played by the nasal mucous membrane and its reflexes in pathology. A brief account of the present view held by rhinologists as expressed, *inter alia*, by Jurasz, will therefore have a certain amount of interest.

Furnished with an abundance of sensory and easily irritated nerves, the nasal organ performs, by means of reflexes, a number of its most important tasks in respiration. The reflexes are produced and regulated by physiologic irritation, the consequence being that before it reaches the lungs the air inspired is warmed, supplied with moisture, and freed from injurious pollution. The nasal organ further represents a protective apparatus for the organism, guarding it, by means of its reflex operations, sneezing, coughing, spasm of the glottis, and cessation of respiration, against gases that are injurious and dangerous for the body. This reflex mechanism, whose operations are of an entirely physiologic nature, may also, however, through the numerous connections between the nasal organ and other parts of the body, produce morbid results, if the nasal mucous membrane for some reason or other becomes abnormally sensitive. It is then no longer the normal physiologic reflex with which we have to do, but the pathologic reflex action, the reflex neurosis. Notwithstanding that the mucous membrane of the nose is continually exposed to injurious influences of various kinds, and in consequence is frequently the subject of pathologic changes, it nevertheless appears that reflex disturbances are comparatively rare. It has been supposed that on account of the resistance of the

nerves to the pathologic irritant, the local changes are not as a rule capable of exerting the necessary stimulus. If, on the other hand, in consequence of local or general nerve weakness, there is also an increased irritability, this favors the transfer of the stimulus to the reflex paths. Thus in addition to the local irritant, another important etiologic factor is required, namely, the increased irritability of the reflex mechanism. The excessive irritability may appear either as a local disturbance or as part of a general neurosis. Sensory stimuli, which are capable of starting reflex neuroses, originate most frequently in the nasal mucous membrane itself. Practically all diseases or abnormalities of the nasal and subordinate cavities, however, will come under consideration here, as every pathologic process is capable of irritating the sensitive nerves, so that reflex phenomena may be produced in cases where the other conditions are also present.

Reflexes are set up most frequently by mechanical irritation of one kind or another. Hopmann attaches special importance to the transitory swelling of polypi and hypertrophic parts of the turbinated bones, particularly if moreover the nasal lumen is contracted as a result of septum deviation, ridges or spurs. Kjelman has reported two cases in which he believes that epileptiform attacks have been caused by changes in the nasal mucous membrane. The same writer found in the special literature 15 instances in which epileptiform attacks are said to have diminished after intranasal treatment. He also considers as chief causes polypi and hypertrophic turbinated bones, especially swollen lower turbinated bones. Tumors that quite fill the nasal cavity seldom give rise to nasal reflexes. Corpuscular elements, such as dust, smoke and vegetable substances, and in some cases the scent of flowers of various kinds, also play a part. In addition to the nature of the irritant, there is also significance in the power with which it acts. In hyperesthetic patients, however, a minimal irritation will suffice to set up the reflex. It is an interesting fact that cases of atrophic rhinitis, unlike those of hypertrophic catarrh of the mucous membrane, are rarely complicated with reflex neuroses, probably because it is accompanied by degeneration of the nerve fibers.

Traumatic lesions, especially after intranasal operations,

also have some significance. Thus Rethi reported cases in which spasm of the glottis and supraorbital neuralgia supervened after cautery and snaring operations. Aronson observed asthmatic attacks after galvanocauterization of nasal polypi. In the literature on the subject, moreover, it is now and again stated that fits of unconsciousness, accompanied by spasms in the upper and lower extremities, can be produced from the nasal mucous membrane. Several of these writings are from an earlier period, before cocain was employed as an anesthetic.

The nasal reflex neuroses originate in the same way as all other reflexes through an irritation of the centripetal nerve fibers in the nasal cavity, i. e., of the first and second branches of the trigeminal or of the olfactory nerve. A few authors have indicated certain zones in the nasal cavity which were said to be especially susceptible to irritation. Hack has pointed out, for instance, as excessively sensitive spots, the anterior part of the lower and middle turbinated bones, while other rhinologists consider the dorsally situated part of the septum as such. In some quarters it is maintained that certain reflex phenomena have certain zones of irritation. Torstenssen, for instance, held that in 400 cases of asthma examined, he had found the place of irritation localized to the upper part of the septum. The present view, which is based upon clinical and experimental investigations, is generally that any spot on the nasal mucous membrane may serve as the point of origin of reflex neuroses. In this connection it should be mentioned that so renowned a scientist as Killian holds a different view. With his "Normalfadensonde" he has found that the irritation is not felt equally strongly in all places. The most marked sensitiveness is found in the anterior part of the nasal cavity on the tubercles of the septum and on the anterior part of the inferior turbinated bones. The posterior sections of the turbinated bones and the septum are as a rule less sensitive. As a result of numerous investigations, Killian, in company with other writers, points out that the respiratory mucous membrane with normal sensibility does not give rise to reflex neurosis. Certain predisposing conditions are necessary for this; and only when they are present can the neurosis appear.

Instead of classifying the reflex neuroses on an etiologic basis, the grouping, Killian maintains, ought to be carried out on an anatomic and physiologic basis. In the respiratory field, for instance, he distinguishes between an anterior zone that is innervated from the first branch of the trigeminal, through the anterior ethmoidal nerve, and a posterior zone, supplied from the second branch of the trigeminal, through the posterior, superior and inferior nasal branches coming from the sphenopalatine ganglion. With regard to these two parts, the ethmoidal and the sphenoidal, the cases are not similar. Killian therefore divides the reflex neuroses into two groups, the anterior or ethmoidal, and the posterior or sphenoidal neuroses. The ethmoidal neuroses are the more frequent, as the anterior portion of the nasal mucous membrane is especially exposed to irritants. As a consequence of this, hyperesthesia will be most easily developed here, particularly in the previously mentioned four more sensitive places. Three degrees of the reflex action may be distinguished, (1) the local, which is confined to the region of the nasal cavity itself, (2) the regional, which may also appear in other parts of the trigeminal field, and (3) the widespread reflexes, which encroach upon other nerve areas. The local and regional reflex phenomena make their appearance within the area of the first branch of the trigeminal and especially in the region of the ethmoidal nerves. In irritable conditions of the ethmoidal part of the nasal mucous membrane therefore, itching is observed not only at the irritated spot, but also in the inner canthus, in the median part of the eyelid, in the caruncula lachrymalis, and in the conjunctiva, without these parts themselves being hyperesthetic. The conjunctiva bulbi can be seen to be hyperemic with increased secretion. Even photophobia may occur from intense irritation of the long ciliary nerves. There is also hyperemia of the skin and the ala of the nose, and not infrequently a feeling of weight is experienced in the region of the forehead, with pain in the frontal sinuses (ethmoidal nerve). In addition to these symptoms, Killian states further that distant phenomena in the form of "nasal cough" and nasal asthma in connection with vasomotor rhinitis and hay fever, may occur as a consequence of the ethmoidal irritation. The sneeze reflex is also an ordinary reflex phenom-

non in these conditions of irritation. The anterior ethmoidal nerve has been indicated by Sandmann as the most important "sneeze nerve."

With regard to the sphenoidal neurosis, too, the anatomic conditions must be kept clearly in view. The dorsally situated parts of the nasal cavity and adjacent parts of the pharynx are furnished, as we know, with sensory nerves from the sphenopalatine ganglion. The relation of the nerves to the sphenopalatine ganglion is important. Some of the nerve fibres pass through the ganglion while others go past it. In both cases, however, ganglion fibers are taken up. The ganglion itself must be regarded, according to von Lenhossek's investigations, as a sympathetic ganglion. It is in direct communication, through the deep petrosal nerve, with the sympathetic plexus round the internal carotid. Nerve branches from its multipolar nerve cells follow the sensory nerves to the mucous membrane over the middle and lower turbinated bones and the septum, and end among the epithelial cells of the mucous membrane. As a consequence of this, irritants that attack these parts must, in Killian's opinion, irritate the sympathetic terminal fibres as well as the trigeminus, and thereby produce reflexes that are quite beyond our knowledge. According to Killian, the reflex phenomena produced from the sphenoidal zone are similar in quality to the ethmoidal reflexes.

It will be of special interest to find out the relation of the nasal reflexes to respiration and the action of the heart. We should expect, not least in the case of respiration, to find reflex irritation phenomena, as the centripetal nasal nerves in the service of respiration may be assumed to exert a great influence on the respiratory center. Several writers have subjected this question to a careful examination, and have made series of animal experiments in order to find out how intranasal irritation can influence respiration and heart action.

As early as 1870, Kratschmer had experimented on curarized rabbits. As irritants he employed various kinds of gas and, more especially, tobacco smoke. He arrived at the following results.

In the animal's organism there is a peculiar reflex connection between the nasal mucous membrane on the one hand and respiration and circulation on the other. The sensory paths

of this reflex connection are situated in the trigeminus, the motor paths in those nerves which supply the respiratory muscles and in the vagus. The reflex appears with any irritation of the nasal mucous membrane, especially with that which is produced by various kinds of gas and always manifests itself in an expiration tetanus with expiratory cessation of respiration, accompanied by a closing of the glottis and by slow heart action and increasing pressure of blood in the arteries.

Kratschmer has also made numerous comparative experiments with isolated irritation of the larynx, trachea and lungs. He considers that the reflex from these organs is of no great importance. The above mentioned reflex symptoms are produced from the mucous membrane of the nose and not from the organs below. Reflexes can of course also be started from the larynx, but they behave in a manner different from that described above. The nasal reflexes are set up notwithstanding intracranial section of the olfactory nerve, but do not appear after destruction of the trigeminal. The author considers he has thereby proved that it is the trigeminal that represents the sensory part of the reflex arc. The motor paths are situated as regards respiration in those nerves which supply the respiratory muscles and as regards the heart in the vagus. It is an interesting fact that by electrical irritation of the intraorbital branch of the trigeminal, Kratschmer produces an expiratory cessation of respiration; but this differs from the cessation occasioned by intranasal irritation, in that by the action of the irritant a deep inspiration always occurs first, followed now and then by small, shallow respiratory movements. Electric irritation, moreover, has no effect upon the heartbeats.

Langendorff, too, found that interruptions of respiration came with irritation of the infraorbital branch of the trigeminal, with slight irritation increased breathing activity or cessation in inspiration phase, with stronger irritation expiratory cessation of respiration.

Besides Kratschmer and Langendorff, Holmgren, among others, showed in 1883 that cessation of respiration can be brought about by irritation of the nasal terminal fibres of the trigeminal, and that it is reflex trigeminal action which, for

instance, causes respiration to cease in a rabbit that is held under water (Rosenthal-Falk's experiments).

Knoll, who carried out his experiments on unnarcotized rabbits, found, on the application of strong electric irritation to the infraorbital nerve, that there was an expiratory decrease in the frequency of respiration and finally complete cessation in the expiratory phase. A similar effect has also been found by strong pressure on the skin over the infraorbital region. Knoll maintains the view that not only must a connection be assumed between the sensory paths and the respiratory centre, but that there must probably also be a direct connection between the sensory nerves and the spinal centers which supply the respiratory muscles with motor fibers. If this were not the case, it would be difficult to establish the fact that in an animal in which spontaneous respiration ceased with the section of the spinal cord, a single deep inspiration could be called forth by strong electric stimulation of sensory nerves. Irritation of these sensory paths can presumably cause a direct irritation, not only of the respiratory center itself, but also of the spinal centers for the respiratory muscles. This interference of irritants issuing partly from the respiratory center, partly from the spinal centers concerned, may explain the numerous combinations of increased respiratory frequency and depression of the diaphragm found in animal experiments, where now the one, now the other type of respiration prevails. The respiratory center situated in the medulla oblongata, whose rhythmic action is kept up by the constant flow of blood to it, can on the one hand be excited by psychic or sensory stimulants, and on the other hand be inhibited through the influence of certain nerve tracts, e. g. vagus and trigeminus. The impulses that issue from the respiratory center are transmitted to the respiratory center in the spinal cord. It is probable, however, that the respiratory center may also be exposed to irritation directly from the cerebrum, as the respiratory muscles can, as we know, be voluntarily set in activity.

Sandmann has on the whole come to the same conclusion as Kratschmer; but he found that with slight irritation of the nasal mucous membrane, it was not exactly an expiratory tetanus that occurred, but a cessation of breathing in the

phase at which it had arrived at the moment when the irritation took place. (Reported from Schmiegelow.)

Sandmann has further carried out experimental investigations with animals, for the purpose of a more minute study of the physiology of the bronchial muscles. He came to the conclusion, *inter alia*, that an irritation of the nasal mucous membrane in noncurarized animals caused, in addition to expiratory cessation of respiration, a narrowing of the air passages by contraction of the bronchial muscles. In this way the protection of the respiratory organ against injurious influences is increased and at the same time the removal of mucus from alveoli and bronchi is greatly facilitated. By contraction of the ring of smooth muscular fibre with which, according to Kölliker, the entrance to the alveoli is surrounded, the mucus will be detached and will thus be more easily removed from the infundibulum. This author asserts that by his experiments on animals he has supplied a physiologic basis for the nasal asthma so frequently described in clinical reports. Brodie and Dickson also claim to have proved contraction of the bronchial muscles after intranasal irritation upwards and backwards from the septum. Several other writers express themselves in the same way. Lazarus, who, in his experiments on animals, used curarized rabbits, has employed electric and mechanical (flicking) irritation of the posterior part of the septum and the lower turbinated. He gives the following as the positive result of his experiments. Certain irritants of the nasal mucous membrane reduce reflexly the lumen of the bronchi. The centrifugal part of the reflex arc is to be sought in the vagus, as, after the section of this nerve no effect is obtained, while the increase of pressure in the bronchi again occurs on irritation of the peripheral end of the vagus. The diminution of the bronchi is in all probability due to contraction of the bronchial muscles. Independently of Lazarus, a somewhat similar conclusion is arrived at by Francois-Frank.

According to Killian, Grossmann has also shown, by experiments on curarized, artificially breathing animals, that electric and mechanical irritation of the nasal turbinated bones in the region innervated by the second branch of the trigeminal causes considerable functional disturbance both of the heart action and of the respiration. There occurred, for instance,

stasis in the pulmonic circulation, increase of the intrathoracic pressure and depression of the diaphragm. The reflexes are supposed to go from the sensory nasal nerves to the central nervous system and thence through the vagi to the heart and lungs and through the phrenic nerves to the respiratory muscles. In noncurarized, spontaneously breathing animals, the irritation caused labored inspiration, which almost led to complete suspension of respiration. The same thing occurred with section of the two vagi. Grossmann therefore thinks, with Koblanck and Röder, that the reflex must have taken another direction, which Killian believes will be found in the sympathetic system. Möllgaard, in 1910, made minute investigations of the respiratory nervous system in vertebrate animals. He confirms the view held in accordance with physiologic research, that the vagus carries bronchomotor nerves to the lung, but at the same time points out that these are of a sympathetic character, as they are interrupted in the ganglion nodosum.

Upon the basis of the above investigations and others which will not be described at length in this brief survey of the literature, it has been thought that the influence of some of the nasal reflex neuroses upon the respiratory organ may be explained in the following manner, namely, that the centrifugal paths which are irritated through the respiratory center will be found in the spinal accessory for the spasm of the glottis, in the spinal nerves of the expiratory muscles for attacks of sneezing and coughing and in the vagus for asthma. There are still many circumstances, however, that are not explained, this being especially the case with regard to asthma. This disease is indeed generally looked upon as a neurosis due to a spasm either of the bronchial muscles or of the diaphragm. Several writers maintain, however, that the asthmatic attacks are due in the first place to a vasomotor disturbance, a vascular dilatation, or a vascular contraction. The general idea, however, as already indicated, is to emphasize the reflex nature of asthma, to regard it as a neurosis originating in sensory irritation of various organs, among them, very frequently, the nose, whether the centrifugal paths are to be found in the vagus, the phrenic or the sympathetic.

The great number of nervous disturbances in the various organs, phenomena which more or less justifiably have been looked upon as nasal reflex neuroses, will not here be described at length. As regards most of these diseases, e. g. Basedow's disease, epilepsy, muscular cramp, neuralgia, migraine, etc., it cannot, according to Jurasz, be proved with certainty that they stand in a reflex connection with pathologic changes in the nasal mucous membrane. There will be special difficulty in deciding what neuroses originate in the nasal mucous membrane, and yet show their result in other organs. It will be clear that the diagnosis in these cases may present great difficulties when it is to be proved that the disease really has originated through irritation of the nasal mucous membrane and in no other way. As Jurasz has pointed out, the physiologic and pathologic experimental investigations that we know of at present, do not yet form a sufficient foundation for a judgment of the clinical phenomena. We cannot therefore disregard the possibility of the influence of other etiologic factors. It must be remembered that the presence of a nasal affection does not by any means prove that a reflex neurosis of simultaneous occurrence is of nasal origin. Even if an attack answering to the neurosis can be produced by instrumental irritation of the nasal irritation zones, the character of the neurosis is not thereby proved.

In an epileptic, for instance, an irritation of the nasal mucous membrane may start an attack. The irritability in such a patient, however, is increased throughout the sensory sphere of the nervous system, and of course not least in the nasal mucous membrane, which also under normal conditions is easily irritated. Even if in this case there are intranasal changes it is by no means impossible that the epileptoid attacks may be started from some other place. On the other hand it will always be significant if a neuralgia or an asthma is favorably affected by intranasal cocainizing. Here, too, however, it must be borne in mind that locally soothing medicaments like cocain may show a transitory favorable effect, even if the neurosis does not originate in the nasal mucous membrane. The fact that the phenomena disappear after intranasal treatment has been emphasized by many writers as a proof of the nasal origin of the neurosis. This proof, however, is not

decisive either; for if the nerve centers are under one kind of irritation, a new irritant may be able to reduce or quite remove this state of irritation (Goltz). Thus the disappearance of sciatica has been observed after cauterization of the lobe of the ear, and the cessation of hysterical attacks after cauterization of the clitoris; but no one would on that account think of connecting these organs directly with the nervous phenomena. It will not always do, therefore, to look upon those nervous disturbances which disappear, for instance, after an intranasal galvanocauterization as nasal neuroses.

Suggestion, too, of which the great importance to the functional neuroses is generally recognized, has also undoubtedly played a great part here. This has especially been the case during that period in which a large number of ailments were said to be curable by means of galvanocauterization of the nasal mucous membrane. Jurasz recalls the constant relapses that take place as soon as the effect of the suggestion has passed away. The treatment is therefore not a decisive proof. There are numerous factors moreover that must be taken into account, such as mechanical conditions, disturbances of circulation, etc., which assert themselves in connection with the treatment given. In general a critical judgment of the symptoms in each case will be necessary in order to avoid being thrown quite off the scent.

From this account of the nasal reflex neuroses it will be seen that it is first of all those reflexes which originate in the nasal mucous membrane itself that have been carefully investigated. On the other hand we have little knowledge of the reflex effect that may possibly come from the antrum mucous membrane. Our literature on the subject does, indeed, give accounts of some cases in which the antrum reflex is supposed to have played a part; but these depend only upon suppositions which as yet lack the necessary experimental physiologic basis. If, however, an attempt is to be made to find an explanation of the symptoms which were observed by me and others in connection with antrum puncture and subsequent injection of air or syringing, this basis must be furnished. The laborious road through animal experiments must be trodden; and if the experiments by irritation of the mucous membrane of the antrum succeed in producing phenomena

similar to those described in the histories of cases, the problem will have been brought nearer to its solution.

An account will be given in the following pages of a series of experiments on animals and their results.

THE EXPERIMENTS ON ANIMALS.

These were carried out on rabbits, as the rabbit has a comparatively well developed maxillary antrum. It appears generally as an irregular cavity about 1.5 to 2 cm. long, 1 to 1.5 cm. high and from 0.5 to 0.6 cm. wide, which aerates the greater part of the maxilla. The antrum is bounded behind by the orbit and the ethmoturbinate bones and is connected with the nasal cavity by an oval opening from 1 to 2 cm. and about 1 mm. wide, situated at the back of the middle nasal fossa, between the maxillo- and nasoturbinal.

As a rule Belgian rabbits were used, of from 2,500 to 3,000 gm. weight. It was found that the use of smaller animals was impractical, as the small space in their antrum made the experiments difficult. The mode of procedure was as follows. The animal was narcotized in the first experiments with ether, subsequently with subcutaneous injections of urethan in doses of 1 gram of urethan per kilogram of body weight. The narcosis that supervened in the course of from 5 to 10 minutes was considerably quieter after this mode of procedure than after the ether narcosis and was borne well. As soon as the animal was narcotized the carotid on both sides was prepared and laid bare for about 1 centimetre, after which a carotid canula was inserted for the registration of the heart action and the blood pressure. For the measurement and registration of the blood pressure a membrane manometer of the Frank type was employed, its movements being calibrated by the aid of a quicksilver manometer. The respiratory movements were also transferred to the registering apparatus by the aid of a pelotte which was fixed by means of an elastic bandage to the animal's abdomen in the region of the diaphragm. In this way exact control of the pulse and respiration was kept and at the same time the blood pressure could be read at any time during the experiment.

It will be remembered from the cases described that the alarming phenomena in the patients did not appear until after

the puncture had been made and in most of the cases in connection with the subsequent injection of air. It was therefore obvious that the same method of procedure should be employed with the animals experimented on, namely, first to puncture the antrum and then see what effect the injection of air would have.

The puncturing of the antrum was performed in the following manner. After the soft parts and the periosteum had been pushed aside, the bony walls in the upper part of the maxillary sinus about 7 mm. below the orbital margin and about 3 to 5 cm. laterally from the median line were perforated with a specially constructed blunt perforator, without injuring the mucous membrane within. After the bone had been perforated in this way, the mucous membrane was pierced with a sharp paracentesis needle, or opened with a fine galvanocautery. A short canula was then inserted, which only just projected into the lumen of the sinus, and which exactly fitted the opening, thus being firmly fixed in the bony wall. For the injection compressed gas was used from cylinders with a regulating valve. With this experimental arrangement the air passed without difficulty into the antrum and out through the ostium maxillare. The injection was done with a pressure of about one atmosphere. It must be remembered, however, that on account of the escape of the air through the maxillary ostium while being injected the pressure in the antrum itself is considerably less than one atmosphere. In order to ascertain this, the following experiment was made. In one of the animals experimented on, two trephine openings were made on the same side. One of these openings was connected with a mercury manometer, and the other with the compressed air receptacle. It proved that the pressure in the cavity did not exceed 200 mm. Hg. By way of comparison it may be stated that the pressure in the antrum in a human being during forced expiration through one-half of the nose may rise to about 120 mm. Hg. If the antrum, through an opening in the alveolus, is connected with a mercury manometer, this can be easily ascertained.

At first the animals were not tracheotomized. It appeared, however, that the pressure of the air through the ostium maxillare was also transmitted down through the trachea. In

subsequent experiments, therefore, a closed canula, airtight towards the cavity of the mouth, was inserted in the trachea, so that all passage of air to the lungs was impossible.

Several of the earlier experiments with animals must be left out of consideration on account of one particular defect in the experiment arrangements, which will be mentioned more fully later on. Only those experiments that were considered to be quite perfect will be mentioned here.

Experiment No. 1.

Rabbit's weight 2,500 grams.

Urethan narcosis with subcutaneous injection of 2 grams. urethan. Antrum canula in left maxillary sinus. Blood pressure at beginning of experiment 99 mm. Hg. Frequency of respiration 24 per minute. Strong and regular respiratory movements. Air was introduced into the antrum 19 times under a pressure of one atmosphere. In the first seven injections, the animal was not tracheotomized.

1. Injection of air during 7 sec. Irregular and superficial respiration and trifling lowering of blood pressure. Pause of 40 sec. Normal respiration and blood pressure of 99 mm. Hg.

2. Injection of air during 7 sec. Cessation of respiration in inspiration phase with two small irregular respiratory movements. Distinct lowering of blood pressure. Pause of 2 min. Regular respiration and blood pressure of 99 mm. Hg.

3. Injection of air during 14 sec. Complete cessation of respiration and lowering of blood pressure for corresponding period of time. A single respiratory movement during the injection was accompanied by a rise in the blood pressure. Pause of 24 sec. Respiration strong, although somewhat slower than before, four in 10 sec.

4—8. Injection of air during four short periods with corresponding irregular, suspended respiration and lowering of blood pressure. Every lowering of blood pressure was followed by a rise as soon as the current of air ceased to flow. Pause of 3 to 4 min. during which tracheotomy was performed and a closed trachea canula inserted. The respiration, which before the tracheotomy was as strong and regular as at the beginning of the experiment, after the opening of the trachea became somewhat irregular and rapid, six in 10 sec.

9. Injection of air during 15 sec. Three small, irregular respiratory movements followed by 10 sec. expiratory cessation of respiration. Pause of 65 sec. Respiration strong, at first somewhat slow, but during the latter part of the pause of normal frequency, five in 10 sec.

11. Injection of air during 10 sec. Absolute expiratory cessation of respiration for 8 sec. and then one shallow respiratory movement. Pause of 25 sec. Strong, regular respiration.

12. Injection of air during 20 sec. Shallow respiration, but no cessation. Pause of 30 sec. Strong, quiet respiration.

13. Injection of air during 15 sec. Shallow, somewhat slow respiration, but no cessation. Pause of 40 sec. Respiration strong and quiet.

14. Injection of air during 16 sec. Expiratory cessation of respiration, and three slow, shallow respiratory movements. Pause of 32 sec. Quiet, strong respiration.

15 to 18. Injection of air during four successive periods, each of 3 seconds' duration, with corresponding irregular, shallow respiration. Pause of 23 sec. Strong, quiet respiration.

19. Injection of air during 7 sec. Four slight, irregular respiratory movements. Pause of 56 sec. Quiet, strong respiration.

20. Injection of air during 15 sec. Respiratory movements somewhat shallow, with decreasing frequency, four instead of six in 10 seconds.

The canula was finally transferred to the trephine opening in the right antrum, where the perforation of the bone had caused bleeding from the mucous membrane. As soon as the pressure was applied, general spasms ensued and death.

The body was dissected immediately after death had taken place. After all the trunk vessels from and to the heart had been ligatured, the heart was first examined. It then appeared that air bubbles were visible through the wall in the right antrum and ventricle. The heart was opened under water in order that the air bubbles might be more easily seen. The right auricle and ventricle were found full of air bubbles and frothy blood, while on the other hand no air was to be found in the left half of the heart. The cranium was then opened

and the cerebral matter examined under water. No air bubbles could be discovered. In the other organs there was nothing special to be noticed.

In this experiment a comparison of the respiration and pulse curves before and after tracheotomy is of particular interest. The respiratory movements, especially during the first half minute after the opening of the trachea, are irregular and shallower than before tracheotomy. It is not long, however, before the animal adapts itself to the new conditions, and the breathing once more becomes regular and strong, although the summits in the respective curves are not so high as during the first part of the experiment. It is further noticeable how different is the effect of the injection of air into the antrum before and after the opening of the trachea. Before tracheotomy the cessation of respiration occurs in the inspiration phase, accompanied every time by a marked lowering of the blood pressure. After tracheotomy there is also, it is true, cessation of respiration, but of quite a different character. It is then really an expiratory cessation of respiration, and this is not accompanied by a lowering of the blood pressure. The blood pressure remains throughout at from 95 to 100 mm. Hg., quite independently of the effect of the air on the antrum.

How then are the cessation of respiration and lowering of blood pressure in the non-tracheotomized animal to be explained? In order to find out, the following experiment was made. A T-canula was placed in the trachea and connected with a water-manometer. It then appeared that the pressure of the air in the trachea, which, during quiet respiration, answered to 2 to 3 cm. water, rose, during the injection of air into the antrum with a pressure of one atmosphere, to from 12 to 14 cm. water. There is thus an increase of pressure of about 10 cm. water, a pressure that is sufficiently great to inflate the lung alveoli in the rabbit, so that a cessation of respiration ensues. The inflation of the lung alveoli with the consequent compression of their blood vessels will be followed by an immediate lowering of blood pressure. In order to test the correctness of this experiment, a closed bent canula was inserted above the T-canula, and through it air was injected with constantly increasing force, until cessation of respiration and lowering of blood pressure occurred. The smallest air

pressure required to obtain this result answered to from 10 to 12 cm. water, a pressure that was read off in the first experiment. It will be seen from these two experiments that the current of air through the ostium maxillare does not only move forwards out through the nostrils, but also backwards down through the trachea, and that the pressure of air here is sufficiently great to cause a cessation of respiration. In all the subsequent experiments with injection of air, therefore, the animals were tracheotomized with closed canula.

Even after tracheotomy was performed, however, it appeared that every injection of air into the antrum distinctly affected the respiration. Four out of the twelve antrum injections with closed tracheal cannula caused absolute expiratory cessation of respiration. The eight other injections were not, it is true, followed by absolute cessation of respiration, but the effect on the breathing was nevertheless marked. It was shown that the respiratory movements with the last three injections of air, although they do not cease, are yet undoubtedly affected. They become irregular and shallow.

Experiment No. 2.

Rabbit's weight 3,000 grams.

Urethan narcosis by subcutaneous injection of 3 grams urethan. Tracheotomy with closed tracheal canula. The antrum canula in left maxillary sinus. Blood pressure 96 mm. Hg. Respiratory frequency 30 per minute. Respiratory movements regular and strong. Air was introduced 10 times into the maxillary sinus with a pressure of one atmosphere and gave the following results.

1. Injection of air during 10 sec. Slow, shallow respiratory movements. Pause of 15 sec. Respiration considerably stronger.

2. Injection of air during 8 sec. Absolute expiratory cessation of respiration for the same period. The cessation of respiration terminated with a convulsive respiratory movement. Pause of 42 sec. Quiet, strong, but rather slow respiration.

3. Injection of air during 10 sec. Absolute expiratory cessation of respiration for that period, followed by two convulsive respiratory movements. Pause of 20 sec. Strong, quiet, but somewhat slow respiration.

4. Injection of air during 30 secs. Absolute expiratory cessation of respiration for 13 sec., and then one convulsive and three irregular respiratory movements followed by 10 sec. of absolute expiratory cessation of respiration. Pause of 16 sec. Strong, somewhat slow respiration.

5. Injection of air during 19 sec. A convulsive respiratory movements. Pause of 10 sec. Strong, quiet respiratory movement the instant the pressure was applied, and then shallow respiratory movements. Pause of 64 sec. Respiration during the first part of the pause somewhat irregular, but gradually becoming strong and regular.

6. Injection of air during 18 sec. One convulsive respiratory movement followed by feeble, irregular respiration. Pause of 62 sec. Strong, regular respiration.

7. Injection of air during 12 sec. Absolute expiratory cessation of respiration for 5 sec., followed by shallow respiratory movements. Pause of 10 sec. Strong, quiet respiration.

8. Injection of air during 10 sec. Absolute cessation of respiration during that period. Pause of 60 sec. Respiration irregular and somewhat suspended.

9. Injection of air during 10 sec. Absolute expiratory cessation of respiration during that period. Pause of 60 sec. Respiration somewhat irregular and suspended.

10. Injection of air during 12 sec. Absolute expiratory cessation of respiration during that period, followed by several convulsive respiratory movements. Pause of 3 min. Bad, irregular respiration. Several intervals with entire cessation of respiration. In the latter part of the pause, however, the condition somewhat improved, the respiratory movements becoming more regular although weaker than before. The capula was now transferred to the other side, where a little bleeding had occurred during the trephining, in consequence of lesion and possible detachment of the antrum mucous membrane. Air emboli were therefore to be expected here, and the instant the current of air was turned on, respiratory spasms did occur with general clonic movements in the muscles of the face and extremities, and the animal died in the course of a few seconds. Autopsy showed the same results as

in the first animal experiment, namely, air bubbles and frothy blood in the right antrum and ventricle, but on the other hand air was not visible in the left half of the heart.

A complete survey of the experiment shows the following results. The animal was of sound constitution, with strong, regular respiration and relatively high blood pressure, 96 mm. Hg. Each injection of air is shown in the curve. As a rule, in seven out of ten cases, absolute expiratory cessation of respiration was caused, lasting, in most instances, as long as the pressure in the antrum was kept up, and being finally succeeded by one or two convulsive respiratory movements, or the respiratory movements continue unchanged, quiet and regular, as soon as the pressure ceased. Three times there was no cessation of respiration. As the pressure was applied, a single convulsive respiration was observed, followed by one or more shallow respiratory movements, after which although the irritant continued to act, the respiration went on quietly without being further affected.

While thus the injection of air exerted an undoubted influence on the respiration, it does not appear to have the slightest effect on the action of the heart. The pulse curve remains throughout quite unchanged. This is also the case with the blood pressure, which was measured at about 95 mm. Hg. as long as the experiment lasted.

Experiment No. 3.

Weight of rabbit 2,500 grams.

Urethan narcosis with subcutaneous injection of 2 grams. urethan. Tracheotomy with closed canula. General condition of the animal good, with respiratory frequency of 48 per minute, and blood pressure of 100 to 110. The pulse curves, during the greater part of this experiment, could not unfortunately be registered, as the blood in the right carotid, notwithstanding every precaution, repeatedly coagulated.

1. Injection of air during 14 sec. One convulsive respiration, followed by expiratory cessation of respiration for 20 sec. only broken by a couple of irregular respiratory movements. Pause of 20 sec. Strong, regular respiration.

2. Injection of air during 14 sec. Three irregular, slow respiratory movements. Pause of 53 sec. Strong, somewhat irregular respiration.

3. Injection of air during 14 sec. One convulsive respiration followed by absolute expiratory cessation of respiration. Pause of 48 sec. Strong, somewhat irregular respiration.

4. Injection of air during 14 sec. One convulsive respiration, followed by absolute expiratory cessation of respiration. Pause of 30 sec. Strong, quiet respiration.

5. Injection of air during 16 sec. Absolute expiratory cessation of respiration during that period. Pause of 27 sec. Quiet, strong respiration.

6. Injection of air during 17 sec. Expiratory cessation of respiration and irregular respiration. Pause of 25 sec. Quiet, strong respiration.

7. Injection of air during 12 sec. Expiratory cessation of respiration and irregular respiration. Pause of 20 sec. Strong, quiet respiration.

8. Injection of air during 8 sec. One quick, convulsive respiratory movement, followed by shallow respiration. Pause of 18 sec. Quiet, strong respiration.

9. Injection of air during 8 sec. One quick, convulsive respiratory movement, followed by expiratory respiration. Pause of 12 sec. Quiet, strong respiration.

10. Injection of air during 5 sec. One quick respiratory movement with expiratory cessation of respiration. Pause of 28 sec. Quiet, strong respiration.

11. Injection of air during 2 sec. One quick, convulsive respiratory movement, followed by a brief cessation of respiration. Pause of 1 1/2 min. Respiration somewhat irregular, as the animal was coming to, for which reason ether narcosis.

12 and 13. Injection of air during 1 sec. and, after renewed pause of 60 sec., 20 sec., gives the same result as before, namely, convulsive respiration and expiratory cessation of respiration.

As the general condition of the animal was very satisfactory, another series of experiments was also made; but these will not be described here, as their arrangement did not prove to be sufficiently satisfactory. The experiments were subsequently repeated with the necessary precautions, and will be described in detail under Experiment No. 4.

In this rabbit, as in the first two experiments with animals, all the injections of air brought about disturbances in respira-

tion. In nine out of thirteen times, the instant the pressure was exerted there was a very rapid respiratory movement, in which the inspiration and expiration followed one another so closely that the curve summit showed only as a perpendicular line. Immediately after there was a cessation of respiration of an expiratory type, and therefore designated as expiratory. In some instances the respiration ceased before the expiratory phase is completed. This suspension of respiration either continued as long as the pressure was kept up, or was finally succeeded, notwithstanding continued injection, by irregular, shallow, slow respiratory movements. Three times there was cessation of respiration without previous forced inspiration.

A complete survey of all the injections of air shows the following: The injection is followed every time by more or less pronounced respiratory disturbances. These are of various kinds. (1) One forced inspiration occurs, followed by one or more superficial respiratory movements. (2) The respiratory movements become slow and irregular. (3) Expiratory cessation of respiration ensues (24 out of 35 times). This cessation of respiration, which may be prefaced or concluded by one or two convulsive respiratory movements, continues without interruption as long as the irritation operates, or it may be succeeded by small, irregular respiratory movements. The irritation caused by the injection of air has no serious consequences for the animal. If the injection is continued for a sufficiently long time, the respiration begins once more, notwithstanding the continued pressure. The pulse does not seem to be affected in any way.

In the experiments hitherto described, air in the form of nitrogen gas has been used as the irritant. This mode of procedure has been adopted because, acting on clinical experience, it was natural to try the effect of a strong air pressure in the antrum upon the animal experimented with. It is evident, however, that the mode of procedure adopted has its weak point simply because we do not know with certainty whence the reflex comes. The air is injected into the antrum, but issues thence through the ostium maxillare and distributes itself over large areas of mucous membrane both inside and outside the nose, areas which may be the origin of reflexes. It appears, however, from Kratschmer's investigations, that

the expiratory cessation of respiration through the employment of gaseous irritants is started intranasally, and not from the lower down in the respiratory tract. The lower parts of the tracheal mucous membrane do not come under consideration here, as the animals were tracheotomized and the trachea firmly attached by ligature to the T-canula, so that all further advance of the air was precluded. It is therefore allowable to take for granted that it is an intranasal and not an extranasal reflex activity with which we here have to do. The question then is, from what part of the intranasal trigeminal region has the irritative effect issued? On this point we cannot, indeed, find out anything certain from the experiments up to the present reported. What we do know is that the atmospheric pressure in the antrum has been measured at 200 mm. Hg., while the pressure in the trachea has fallen right down to 12 centimeters water. We should therefore be able to take for granted that also the pressure in the nasal cavity itself is far less than within the antrum. It is in the antrum that the pressure has acted with its full force, and it is therefore probable that the reflex has come from the part of the trigeminal that is situated there.

Any doubt as to the possibility of reflex respiratory disturbances being set up from the mucous membrane of the antrum will disappear, however, from the result of the last animal experiment, which above all forms the foundation of the experimental part of this work.

It will be remembered that the clinical experience upon which the animal experiments were based was all connected with the treatment of diseased antra. In the experiments, however, we have had to do only with healthy antra. When we consider how very much more sensitive the inflamed mucous membrane of the antrum is than when in its normal condition, we must be justified in attributing a certain importance to this circumstance. Nor can we altogether ignore the fact that the animals were narcotized and therefore without feeling of pain. Knoll, who has experimented on animals both with and without narcotics, maintains, indeed, that the reflex action is the same. He has found no fundamental difference, but the simultaneous effect of the sensitive "*Erregungen auf die Psyche*" seems to condition an increase in the

reflexes from the respiration when the animal is not narcotized. The factors mentioned both go to show that other, possibly stronger stimuli should be tried, stimuli which, unlike the air injected, only exerted their irritative effect where they were applied. There is also another circumstance which should be mentioned in this connection. In going through the literature it was stated that some scientists have produced an effect upon the respiration by irritation of the nasal mucous membrane itself, an effect that in most cases manifested itself as an expiratory cessation of respiration. Thus far my results agree very well with earlier experiences; but when it comes to the reflex effect on the heart action it is a different matter. Here most writers have found marked vagus effect. During the injection of air, on the contrary, the heart's action, as already mentioned, did not appear to be affected. In any case the pulse curve shows no change, no sign of vagus effect. The blood pressure also remains unchanged. It might be imagined, however, that a specially powerful stimulation of the sensory trigeminal fibres in the antrum might also manifest itself as influencing the heart action in the direction indicated by earlier writers.

In accordance with what has here been pointed out, experiments were made with chemical stimuli, alcohol, ether and tincture of iodine. All these substances have in common the unfortunate property of destroying the mucous membrane, and thus making further experiments impossible. The application of these stimuli in the maxillary antrum is, however, easy and rapid in performance. They were nevertheless chosen. As there was an *a priori* reason for taking for granted that they would be capable of exerting an especially powerful irritative effect, and that this effect would presumably originate in the place of application.

Experiment No. 4.

Weight of rabbit, 2,100 grams.

Urethan narcosis 2 grams. Closed canula in the trachea, and antrum cannula in both maxillary antra. General condition of the animal excellent, with blood pressure of 130 mm. Hg. Respiration rather rapid, 48 per minute, but strong and regular throughout the experiment. 96 per cent of alcohol

and ether alternately was used as stimulus, 1/10 of a Pravaz syringe each time.

Alcohol in the right maxillary antrum produces instantly a violent reaction. There was first an absolute cessation of respiration for eight seconds, only interrupted by one convulsive inspiration, and then complete respiratory tetanus with a long series of convulsive respiratory movements, which did not cease until 35 seconds had elapsed. During the brief absolute cessation of respiration which concluded the irregular respiratory movements, the death of the animal was momentarily expected. This expectation, however, proved to be wrong. Respiration soon started again, and with as regular and strong respiratory movements as before the application of the irritant in the maxillary sinus. It was very interesting to find that during the respiratory paralysis there also occurred general paralysis with violent jerks in all the extremities and in the muscles of the face.

Of no less interest is a study of the blood pressure and the pulse curve after the alcohol injection. Whereas, the blood pressure, in all the previous experiments with injection of air, had remained unchanged and quite unaffected by the respiratory disturbances, this time we find a tremendous increase in the pressure of the blood, rising from 130 to 179 mm. Hg., an increase of 49 mm. Hg. The blood pressure remained high all through the respiratory spasm, but showed a somewhat falling tendency, so that when the respiration began once more, it was measured at 155 mm. Hg. The pulse curve, too, changed considerably after the alcohol injection. The pulse beats at first became slower, then small and irregular, and finally, during the greatest rise in the blood pressure, seemed to disappear altogether. During the spasms the pulse curve appeared as an almost straight line; but as soon as the convulsive stage was past and the respiration starts again, the pulse beats were once more seen in the curve, which acquired the same appearance as it had before the injection.

Throughout the pause of about two minutes which followed the alcohol injection, the respiration was strong and regular. The blood pressure remained relatively high, but fell by degrees to 142 mm. Hg. Alcohol was then injected into the left nasal cavity. In order to avoid injuring the mu-

cous membrane in the vestibule of the nose, which in the rabbit is very narrow, the nozzle of the springe was carefully guided 1 cm. into the nasal cavity, where the injection was made. Irregular respiration immediately began, but did not last more than three or four seconds, and did not seem to affect the animal in any way. After a few seconds the respiration continued quiet and strong as before. The rise in the blood pressure, however, which occurs immediately after the ether injection, is worthy of remark. The pressure rises from 142 to 166 mm. Hg., an increase of 18 mm. Hg. The blood pressure remains at this height for 28 seconds, and then falls again to 152 mm. Hg. On this occasion, too, the pulse curve loses its usual appearance and shows as an almost straight line.

After a pause of two minutes with quiet, strong respiration and a blood pressure which measured, at the end of the pause 123 mm. Hg., ether was applied to the left antrum.* Expiratory cessation of respiration for five seconds immediately occurred, and a rise in the blood pressure of 14 mm. Hg., from 123 to 137 mm. Hg. During the subsequent 1½ minute's pause the respiration again became strong and irregular. The blood pressure measured 134 mm. Hg.

Ether in the right nasal cavity produced a convulsive respiratory movement, but did not affect the blood pressure.

After a pause of 50 and 60 seconds, ether and alcohol were again injected respectively into the right and left antrum, without appearing to affect the respiratory movements or the blood pressure in any way. The respiration continued unchanged, strong and regular, and the blood pressure was measured at 130 mm. Hg. until the experiments were discontinued.

The fact that the antrum mucous membrane did not react for stimuli after the first experiments is probably to be accounted for by the destruction of the ends of the nerves in the epithelium of the mucous membrane by the alcohol and ether injections.

*The small quantity of ether can be supposed to be evaporated after having been injected into the warm antrum. It is therefore possible, that there has been a more or less pronounced refrigeration, which cannot be compared to the strong irritation, caused by the alcohol.

In contrast with the first three experiments with animals, chemical stimuli have here been employed, namely, alcohol and ether. These were applied in the antrum and nasal cavity in the following order: (1) Alcohol in the right antrum, (2) alcohol in the left nasal cavity, (3) ether in the left antrum, (4) ether in the right nasal cavity, (5) ether in the right antrum, (6) alcohol in the left antrum. The experiments show that in this rabbit alcohol produced the more violent reaction and that the reactive effect was very much more pronounced with the application of the stimulus to the antrum than with injection into the nasal cavity; but also with the latter mode of procedure the effect, especially on the blood pressure, was indubitable. On the other hand, the reaction after the ether injection was not very marked, no change being found, for instance, in the blood pressure.

In this animal, as in the others, death was caused by air emboli when the air was injected between the antrum mucous membrane and the underlying bony wall.

For purposes of control, alcohol and ether were dropped into the antrum of another rabbit. The experiment will not, however, be reported in detail, because, among other reasons, the blood in the carotid canula coagulated, and therefore the pulse and the blood pressure could not be registered. I will only emphasize the fact that the effect on the respiration was pronounced (cessation of respiration), although of not nearly so violent a character as described above after the application of alcohol to the right antrum.

The four animal experiments here described, which should be viewed from one standpoint as a collected whole, will be sufficient to prove that by irritation of the mucous membrane of the antrum in the rabbit disturbances in respiration and blood pressure can be produced. These, however, are not dangerous for the animal when only injections of air are employed as stimulus; but if stronger stimuli, such as alcohol, are used, alarming phenomena will appear. In addition to the most violent disturbances in the respiration, tonic and clonic spasms may occur in the muscles of the face and extremities, and also a marked rise in the blood pressure.

The question now arises, how are these symptoms to be explained anatomically and physiologically?

The anatomic conditions which especially come under consideration in the intranasal neuroses will first be briefly mentioned. Figs. I and II. The maxillary antrum, as we know, receives its sensory innervation from the superior alveolar nerves, branches from the infraorbital nerve, which is one of the main stems of the second division of the trigeminal. This divides in the sphenomaxillary fossa into the infraorbital nerve and some other branches, of which the sphenopalatine nerves will be of special interest in this connection, for the sphenopalatines represent the sensory roots of the sphenopalatine ganglion, which is regarded by anatomists as a sympathetic ganglion, and is in direct connection with the plexus of sympathetic nerves round the internal carotid.

When it is a question of find out the way or ways that an irritation of the alveolar nerves may be supposed to take, attention must not only be directed to the principal way through the second branch of the trigeminal to the ganglion semilunare and on to the brain, but must also be turned to the nerve tracts to the sphenopalatine ganglion and the sympathetic system.

If the first way is followed, to the ganglion semilunare, where the cells of the sensory trigeminal fibers are situated, the following anatomic conditions must be kept in view. From the sensory trigeminal cells in the ganglion semilunare run centripetal filaments, sensory fibers of the first order, through the portio major into the brain. Here the fibers divide in the form of a T into a short ascending and a long descending branch. The descending branches form the so-called spinal tract of the fifth nerve. It runs right down to the upper part of the cervical spinal cord. In their course both the ascending and the descending branches send out numerous collaterals, which wind round the nerve cells grouped together upon their median side. These cells form in the pons a large nucleus, the so-called sensory nucleus of the fifth nerve; caudally they form the previously mentioned nucleus of the spinal tract of the fifth nerve. From these nerve cells issue the sensory fibers of the second order, the nerve offshoots that form the great quintothalamic tract, and which end in the thalamus, where the sensory neuroses of the third order running to the cortex have their origin. In what relation, then, do these sensory

offshoots from the trigeminal nucleus stand to the respiratory center?

The earliest idea, that the respiratory center, "neud vital," formed an asymmetrical center in the posterior angle of the calamus scriptorius, has now been abandoned, but its position in the medulla oblongata has not yet been established with certainty.

While some scientists place it in the reticular substance, especially the lateral gray reticular substance, others are of opinion that it is to be found in the ala cinerea area, or in the dorsal vagus nucleus and the nucleus of the solitary tract, situated in the floor of the fourth ventricle.

Great confusion has also prevailed regarding the course of the tracts that connect the respiratory center in the medulla oblongata with the motor nuclei for the nerves of the respiratory muscles, especially the phrenic nucleus and the nuclei of the intercostal nerves in the spinal medulla.

The most important recent work on this last subject is by Max Rothmann ("Ueber die spinalen Athmungsbahnen." *Arch. f. Anatomie u. Physiologie, Physiolog. Abteil.*, Jahrg., 1902).

According to Rothmann, the involuntary respiratory center is to be found in the medulla oblongata in the gray reticular substance. The tracts for the innervation of the diaphragm run almost exclusively through the ventral part of the lateral column, and those for the thorax muscles (intercostal muscles) principally through the lateral part of the anterior column. After the destruction of the reticular substance in the medulla oblongata, these tracts appear to degenerate. Some of them are crossed, some are not. An irritation of the respiratory center will be transmitted through these tracts to the phrenic center and the intercostal nerve centers in the spinal cord, and bring about a contraction of the diaphragm and of the intercostal muscles.

The diagram (Fig. I) shows how near, in the topographic sense, the sensory trigeminal nerves are to the respiratory center. We can imagine an irritation of the trigeminal tracts transmitted to the respiratory center in one of two ways, either by a direct radiation of collaterals from the spinal tract into the respiratory center (reticular substance), or the con-

nection may be more complicated—e. g., the nerve offshoots that issue from the cells in the nucleus of the spinal tract of the fifth nerve, and run upwards to the thalamus, may throw out collaterals to the reticular substance.

It would appear from the above that respiratory disturbances, regarded from an anatomic point of view, may very well be produced by the transmission of an irritation from the trigeminal to the involuntary respiratory center in the medulla oblongata, and thence to the respiratory muscles. What in this instance makes the matter more complicated is, however, that in one of the animals experimented upon, not only were respiratory disturbances proved to occur, but also, in connection with them, general spasms of the muscles of the face and extremities, together with a tremendous rise in the blood pressure.

As collaterals run from the fibers in the quintothalamic tract to the nucleus of the facial nerve, and also, according to the general belief, the reticular substance is united by connecting fibers to the adjacent nucleus of the facial nerve, it will be easily understood that an irritation of the terminal branches of the trigeminal may also cause spasms of the muscles of the face. The fact that the muscles of the extremities were likewise affected seems, however, to indicate that the stimulus, at any rate in this instance, has passed by the quintothalamic tract to the thalamus and thence onwards to the cortical substance, and that it is there, in the brain cortex, that the irritation has attacked the adjacent centers.

It will be remembered that during the injections of air the pulse curve did not show the slightest indication of change in any direction. On the employment of chemical stimuli, on the other hand, especially after the alcohol injection into the right antrum, a tremendous rise in the blood pressure immediately occurred. At the same time the pulse became first slow, then small and irregular, and finally, when the rise in the pressure had reached its maximum, almost entirely disappeared, so that the pulse curve only looks like a slightly undulating line in which the separate pulse beats can only just be distinguished. Very much the same reaction, although not so strong, is also found after an alcohol injection in the left nasal cavity. The great increase in the blood pressure can

only be accounted for in two ways, either by an increase in the work of the heart or by an increased resistance in the circulation. In the first case, the increased heart action throughout the rise in the blood pressure would manifest itself in the pulse curve by strong heart beats and high summits. It appears, however, from the above that this is far from being the case; indeed, the pulse beats in the curve are at last seen almost to disappear. The great rise in the blood pressure therefore cannot well be due to the increased heart activity.

It seems natural, then, to explain the rise in the blood pressure in the second way, namely, as the consequence of an increased resistance which the heart can at first overcome, but which at last becomes so strong that the heart is no longer able to continue its work with such force as to mark the systole in the greatly overfilled arteries, and in consequence the contractions of the heart are no longer recorded in the pulse curve, which appears as an almost straight line. The question now is: How is this increased resistance to be explained in connection with the other reflex phenomena?

One would here naturally think of a reflex irritation of the vasoconstrictor nerves. If we try to find an anatomic basis for an explanation of this reflex activity, the following anatomic conditions must not be lost sight of. The trigeminal branches running to the back of the nasal cavity (posterior superior and inferior nasal branches) pass through the sympathetic sphenopalatine ganglion, and, according to von Lennosse's investigations, send out collaterals which envelope the sympathetic nerve cells in the ganglion. The latter again is in connection with the plexus of sympathetic nerves round the internal carotid. A stimulus that is transmitted through the trigeminal fibers to the ganglion may therefore be supposed to produce a constrictor impulse to the sympathetic plexus round the internal carotid. There seems little reason to suppose that the rise in the blood pressure in the cases before us is due only to a contraction of vessels within the carotid area. The natural explanation would rather appear to be that the irritation from the alveolar nerves has taken the previously mentioned way to the brain cortex, and that it is there that the impulse is transmitted to the vasoconstrictors.

As to how this transmission has taken place it is difficult, with our still imperfect knowledge of the central sympathetic centers and tracts, to express any decided opinion. I will only in this connection point out that according to Tigerstedt there are generally supposed to be two principal centers for the vasoconstrictor nerves. One of these is believed to be situated in the medulla oblongata, where the root fibers of the facial leave the continuation of the spinal cord (Frank), the other within the motor zone of the brain cortex. It thus appears from Weber's experiments that an irritation of the motor sphere in the cortical substance of the cerebrum not only produces ordinary muscle cramp, but is also followed by a distinct effect upon the muscles of the vascular system, the vessels innervated by the splanchnic nerve especially being contracted. Whether there are connecting fibers between the centers mentioned and the adjacent nerve centers in the continuation of the spinal cord, or the brain cortex, is not known as yet. It can only be said that in analogy with the conditions of other adjacent nerve centers where the connection has been anatomically ascertained, it is natural to suppose such connections also between these centers. The experiment before us seems at any rate to favor the idea that a transmission of the stimulus has taken place either in the medulla oblongata, or, as already pointed out, more probably within the motor sphere of the brain cortex around the central sulcus where the chief respiratory center and the motor centers and the vasoconstrictor center are to be found.

It has repeatedly been stated that the majority of investigators have found, after intranasal trigeminal irritation, a marked vagus effect both on respiration and heart action. As, however, in my animal experiments I have never been able to prove a vagus effect on the heart action, I have endeavored anatomically and physiologically to elucidate the phenomena observed, on the basis of the assumption that there has been no vagus irritation. I am, however, fully aware that my explanation of the symptoms is not in all respects entirely satisfactory.

We should have expected, for instance, that if the irritation had taken the course mentioned, through the respiratory center to the intercostal nerves and the phrenic nerve, a con-

traction of the intercostal muscles and of the diaphragm would have been started, and that this would have resulted in an inspiratory cessation of respiration. We get, on the contrary, an expiratory cessation of respiration, a phenomenon which more particularly favors the idea of an irritation of the bronchomotor vagus fibers. It would be remarkable, however, when we consider the whole origin of the motor vagus fibers to lungs and heart (the visceromotor vagus nucleus), if an irritation which affected the center were to exert its influence only on the bronchomotor fibers. It would seem natural for the irritation to be also transmitted to the heart fibers, with vagus effect on the heart as a consequence. With our present very imperfect knowledge of the central conducting paths and their mutual relations, it will hardly be possible to give an entirely satisfactory explanation of the symptoms before us. Nor can we altogether disregard the possibility that this may have been a combined irritation of various nerve centers, an irritation which, owing to conditions unknown to us, in individual cases may act with unequal force upon various centers, and which therefore will give such widely different symptoms that from an anatomic point of view they can hardly be explained.

In connection with the report of the cases it was shown that the sudden and unexpected shock phenomena in the patients might, from a theoretic point of view, as well be ascribed to the anesthetizing as to the operation itself and the subsequent injection of air or syringing. As regards the first alternative it was pointed out that a cocain anesthesia, especially in a nervously disposed patient, who, moreover, owing to the disease, was not very capable of resistance, might well have had significance as a predisposing element, but that the cocain can scarcely have been the decisive factor.

The question then is whether the injection of air or syringing may not have had something to do with the phenomena. To this it may be answered that the symptoms observed during the animal experiments exhibit in a number of points a striking similarity to the phenomena that have been observed both by earlier writers and by myself in connection with antrum punctures. It will be remembered, for instance, that the cessation of respiration was at first the dominant

feature in all my cases. There are further the suggestive occurrences from the motor sphere, which were seen in my cases 1 and 2, in the first case general epileptoid convulsions, in the second a spastic condition of cramp in the trunk and extremities. In this connection it should be pointed out that with these patients there was not the slow, hard pulse mentioned by several writers, and supposed to be the expression of a vagus irritation from the trigeminus. In the three patients in whom there was opportunity of observing it, the pulse during the first part of the attack was uncountable, and afterwards small and rapid.

It thus appears that through irritation of even a healthy antrum mucous membrane, reflex conditions of irritation are produced in the rabbit, which greatly resemble the symptoms which, in man, occurred in conjunction with puncture of the antrum. It therefore cannot be denied that with sensitive persons, at any rate, increased air pressure or syringing, for instance with cold water (cf. Killian's case), may act as a sufficiently strong stimulus to the inflamed mucous membrane of an antrum, to set up reflex irritation phenomena of a serious nature. It happens, however, surely very seldom. As a rule, the alarming antrum phenomena will be interpreted in another, more obvious manner.

In the description of the animal experiments it was stated that some of the experiments failed, especially on account of one particular defect in the arrangement of the experiments. It was the defective technic in the perforation of the bony wall of the antrum which here gave trouble. One animal after another died of air emboli and emphysema. In each case autopsy showed the same result. The trocar had, it is true, perforated the bone, but not the mucous membrane, or at any rate not to a sufficient extent. The mucosa was torn away from the periosteum of the bony wall, the small blood vessels between being injured in consequence, and the air forced into the opened veins, with instantaneous death as the result. It was on the whole remarkable how difficult it was to avoid air emboli. With the facts learned from animal experiments, it was natural to enquire into the conditions in man, whether the mucous membrane here, too, could be so loosely attached to its bony substratum that a careful, slow

puncture such as must, owing to space conditions, be made in the case of the small animals experimented on, might be attended by the risk of detaching the mucous membrane. It is obvious that in man this complication is not of frequent occurrence. If the antrum picture were generally associated with a loosening of the mucous membrane of the antrum, the unfortunate consequences of this simple operation would undoubtedly be far more frequent than is the case. We see, however, that complications occur but seldom. I have myself, for instance, in a single series of investigations, punctured about 50 antra without one mishap. If, however, we wish to make a comparison between the conditions in the animals experimented on and those in man, care must be taken, as already said, that the puncture is performed in the same manner, and that the trocar is not pushed quickly through the wall, but slowly, little by little. It is, as we know, seldom that an antrum puncture is performed in this manner, but it will occasionally happen that the anatomic conditions prove to be such that the puncturing needle's progress is slow, namely, in those cases in which the bony wall in the lower meatus is so thick, and the bone of so firm a consistency, that it is really not possible to push the trocar through quickly. It is only antra where such conditions exist, that is to say, the small, thick walled ones, that can come under consideration here. Keeping these conditions in view, a series of investigations have been made, some on the dead body, others on patients. The antrum in one of the bodies examined was small, and with so thick a wall that it was only with great difficulty that the needle could be made to pierce it. It appeared that in this case the trocar detached the whole of the median mucous membrane of the antrum from its bony substratum, and pushed it in towards the lateral wall surface of the antrum without perforating the membrane. The mucosa was thick and swollen as a consequence of empyema in the antrum.

In the living subject examination was made during the performance of a radical antrum operation according to Luc-Caldwell. After removal of the facial wall, the light was thrown in towards the median wall of the maxillary antrum, simultaneously with the perforation of the bony wall from

the lower meatus. The relation of the mucous membrane to the needle during the operation could be observed with great exactness. In the patients examined the maxillæ were large and the antrum walls easily penetrated. In one of the patients the trocar was quickly and forcibly pushed into the antrum. The mucous membrane was instantly pierced, without any loosening. On the other hand, in another case where the mucosa was thick and swollen, the needle, by way of experiment, was introduced slowly and gradually. It then appeared that the trocar to a large extent detached the mucous membrane from the bone, and pushed it in towards the lumen of the antrum. The mucous membrane was pushed so far in before the perforation took place, that the operator in such a case would certainly take for granted that injection of air and syringing could be performed. It is clear that the result of an injection of air or water in these circumstances might be that the air would be blown into the opened blood vessels between the mucous membrane and the periosteum, and thence carried into the circulation. The question would thus be: What might be the consequences of such an injection of air into the blood? We here enter upon a chapter of medical science in which a considerable amount of uncertainty still appears to prevail.

THE AIR EMBOLUS.

The air embolus, with its dangers, has been the subject of careful research by many writers. It has long been known, for instance, that a forced injection into the veins of an animal may cause death. Harder, as long ago as 1684, injected air into the jugular vein of a dog, which died instantaneously. On dissection, frothy blood was found in the heart. Spontaneous entrance of air during an operation with lesion of the veins was first observed in 1806 by Verrier in a throat operation on a horse. The operative air embolus in a human being was not described until later. In 1824 Dupuytren published an account of one of the best known cases. During a throat operation a sucking kind of noise was suddenly heard and the patient died instantaneously. The postmortem showed air in all blood vessels, especially in the right heart. Since then a number of similar cases have been reported, not only

during throat and thorax operations, but also in lesions of the more peripherally situated venous trunks. The clinical description is very much the same. During the entrance of the air there is heard a gurgling, scraping noise, proceeding from the injured vein. Immediately afterwards a peculiar rattling sound is heard over the heart, where the percussion note becomes tympanitic. At the same time there is more or less irregular respiration, sometimes with convulsive, and sometimes with suspended respiratory movements and with irregular heart action. The patient may die instantaneously or after the lapse of some time, not infrequently in convulsions. Now and then the patient recovers without lasting injury. The results of autopsy do not always correspond. Certain investigators, for instance, have found air bubbles only in the right heart and the large venous trunks, while others claim to have found air in all the blood vessels of the body, at the same time maintaining that this air did not originate in the process of putrefaction. Hübl also found air bubbles in the small blood vessels of the spinal cord. All investigators emphasize the fact that it is primarily in the right heart that the accumulation of air is found. The right half of the heart is described by most of them as tightly filled and inflated like a balloon.

Opinions with regard to the cause of death differ greatly. Some consider that it has been a "lung death." The air is driven out by the right heart into the lung capillaries, which are embolized, and the circulation is interrupted with death as the result. It has sometimes been supposed that the air emboli have become fixed in the small blood vessels of the central nervous system, thereby causing a "brain death." Most writers seem to incline, however, to the view that the cause of death should be looked for in a paralysis of the heart and that thus the death as a rule has been a "heart death."

The numerous experiments on animals that have been made in this connection are of great interest, and on several points contribute valuable material towards the understanding of the air embolus and its dangers.

Theodor Jürgensen has made a great many experiments with dogs. They showed, in every case in which the animal did not die instantaneously, that air that was introduced into

the right crural artery could be traced in the left crural vein, even after the left crural artery was ligatured and the air bubbles were thus forced to pass through the collateral connecting lines. With inspiration, the air bubbles that could be seen in the vein were sucked up towards the heart, while with expiration they stood still or even moved back a little. After the air injections the respiratory movements were rapid, dyspneic. The respiration curves showed steep summits with large oscillations. When death was approaching the curves were still steep, but irregular and slow. In the case of one of the animals experimented on, 530 cc. was injected in the course of 48 minutes, and in another 2,730 cc. in the course of about $2\frac{1}{2}$ hours, without causing any noticeable changes in respiration and heart action. It was proved that the air bubbles circulated for four or five hours.

There seemed to be no doubt that a rapid separation of the air from the blood took place, as it would otherwise be inconceivable that such large quantities of air should not produce more alarming symptoms than was the case. On dissection of the animals that were killed by rapid injection of large quantities of air, air was found in the arteries. The right heart was full of air and very frothy blood, and there was a considerable amount of blood mixed with large air bubbles in the large veins, while as a rule the left ventricle was almost entirely empty. It seems as if this part of the heart has been sufficiently powerful to expel the comparatively trifling amount of air left after passing through the lungs into the circulation. The writer draws attention, however, to the fact that the condition thus discovered by dissection cannot always be expected to occur. If, for instance, a large quantity of air is injected rapidly, so that the right heart is distended and becomes incapable of emptying its contents into the lungs, or if the air is introduced sufficiently slowly and carefully, there will probably be no free air bubbles to be found in the arterial vascular system. Jürgensen, however, considers it sufficiently proved, by his experiments with animals, that air from the right heart can actually be carried through the lungs to the left, and thence into the circulation.

The cause of death by air emboli is also mentioned by

Jürgensen, whose view is in accordance with that maintained by Couty. The latter writer, who has made a number of investigations of the blood pressure in the large vessels, distinguishes between several different groups of symptoms according to the amount of air injected, and believes that death may be caused in several ways.

1. Entrance of air without general disturbances.

After small quantities of air, a few cubic centimeters at once, or larger quantities introduced little by little through the veins, no general disturbances are seen. If the pressure in the large arteries is measured, it will be found to fall a little. Over the heart, too, a peculiar systolic murmur is heard, arising from the air intermingled blood in the right ventricle of the heart. Respiration is not affected.

2. Entrance of air with cerebral anemia.

It must then be presupposed that a large amount of air enters quickly. The consequence will be a lowering of the pressure in the large arteries (40 to 50 mm. Hg.). The systole becomes weaker, the pulse rapid, respiration frequent. In man the face turns pale and syncope ensues, after which all dangerous symptoms as a rule subside.

3. Entrance of air in large quantities, with disturbances in the circulation, especially with anemia of the brain and medulla oblongata.

In addition to the phenomena mentioned under heading 2, respiration is slow and spasms occur in all the striated muscles. In curarised dogs with opened thorax, a dilatation of the right auricle and ventricle is seen as a consequence of the overflowing with air, also venous reflex with venous pulse even in the smallest veins.

4. Entrance of air with disturbances in circulation, especially in the nervous organs.

These are disturbances that result in death. During a rapid lowering of blood pressure the previously mentioned symptoms appear in an intensified degree.

The physiologic basis is the same in groups 1 and 3. As a consequence of the arterial anemia, the brain is paralyzed in its function, and respiration and heart action cease.

In addition to Jürgensen's work, mention should be made, in this connection, of Ludwig Wolf's experimental studies

of air emboli. The last named writer also carried out his experiments on dogs, but as a rule injected the air into the right jugular vein, up to 200 cc. in the course of 45 minutes, in quantities of up to 50 cc. at a time. The animals reacted even with minimal quantities of air in the same way, labored, irregular, intermittent respiration, and irregular but strong pulse. The results of his experiments were as follows: The air introduced into the venous system is quickly conveyed to the right heart, where, even after the injection of minimal quantities of air, a humming sound is heard during compression of the aerated blood by the heart. On the entrance of larger quantities of air, dilatation of the right heart ensues with relative insufficiency and overfilling with air in the large venous trunks. From the right heart the pulmonary artery is filled with bubbles of air, which make their way into the lung capillaries. Beyond this, i. e., in the pulmonary veins and in the chambers of the left heart, Wolf has not been able to prove the presence of air in any great quantity, and maintains that those writers who, after venous emboli, have found air in the entire circulation, have made an error of observation. The air bubbles observed must have originated in processes of decomposition, or in the entrance of air during dissection. Wolf further alleges that the air embolizes the lung vessels, but that the resistance here encountered is overcome by the heart, if at the same time too great a number of capillaries is not blocked. The writer maintains, however, that a few air bubbles may also find their way into the capillaries of the pulmonary veins, and that in this way, through embolizing of blood vessels in the brain and spinal cord, or of the coronary arteries, death may ensue that cannot be called a lung death. He thinks, however, that this is rare. The general cause of death is embolism of the lung capillaries. It is therefore found that the fall of the blood pressure in the aorta is on a parallel with the amount of air injected, while the pressure in the pulmonary artery rises. What has become of the large quantities of air injected in the veins? It is not in the systemic circulation, nor yet in the right heart and the large veins, unless the whole of the pulmonary circulation is suddenly stopped by a great injection of air. The only explanation is that the air has escaped through the lungs. Cohn-

heim, who is an opposer of the theory of the embolic lung death, emphasizes indeed the fact that an animal can live even if only half of the pulmonary vessels are pervious. Wolf refers, however, to Lichtheim's investigations, which show that three-fourths of the pulmonary circulation must be put out of gear if the pressure in the aorta is to diminish, and points out that in those cases in which death is caused by aspiration of air into the vessels, it is probable that far more than half the vessels are embolized.

A number of investigators, among them Wolf, have proved that in an injection of air into the arterial system the air is carried with the blood through the entire system. Air introduced into the crural artery, for instance, is found as previously mentioned, in the crural vein on the opposite side. Heller, Mager and von Schrötter have also described manège moments, paralyses, loss of consciousness, tetanic cramps, spastic paralysis and paraplegia, symptoms which all point to capillary emboli in the systemic circulation. Autopsy showed hyperemia of the lungs and, contrary to what is found with venous emboli, air throughout the circulation. Similar conditions are also found, as Jürgensen has shown, with air emboli issuing from the ventricle and the abdominal veins. According to Wolf, the case of venous emboli from the abdominal vessels differs somewhat from the usual cases of venous emboli; for as the air passes through the capillaries of the portal system it is liable, just as in its passage through the capillaries of the systemic circulation, to an equally strong pressure from all sides, and is in consequence so finely distributed throughout the blood that it can, to some extent at any rate, make its way through the pulmonary circulation. The large air bubbles, which might possibly form on the way to the lungs, do not appear in such numbers as to cause a simultaneous embolization of large sections of the lung, and thereby bring about serious consequences. The lungs form, on the whole, the organism's most powerful defense against the air that has entered into the blood, as they give to the systemic circulation the protection of a rampart. When once the air bubbles have entered the systemic circulation, the danger of serious complications will be considerably greater. They will then embolize vital vessels, with death as the result.

It will be seen from the investigations that I have carried out for the purpose of ascertaining the condition of the mucous membrane during the trephining of the antrum wall, that a loosening of the mucous membrane in special circumstances may very well be assumed to take place. It will further be remembered that in several of the cases described, it is stated that the antrum wall was thick. This was the case with two of my patients, and I had not the usual well known feeling of the bone suddenly yielding and the trocar gliding into a cavity. The resistance was too strong for this. It was supposed that the bone was punctured because the trocar had penetrated so far that even a very thick antrum wall must have been perforated, and because the point of the cannula could be moved a little in various directions. The air was then injected, and a kind of bubbling sound was heard, which might, however, also have been supposed to be made by the air as it made its way under the bleeding mucous membrane. It is noteworthy that with both these patients there was a certain interval between the injection of the air and the occurrence of the phenomena. In the case of the one patient, for instance, the injection of air had ceased, and it was not until the syringe had been transferred to the water receptacle that the symptoms made their appearance. This also seems to favor the belief that it was a case of embolus. How great a quantity of air may have been forced into the vessels cannot be precisely stated; but with neither of the two patients in question was the ball of the syringe compressed more than twice at the most. As the bulb, when filled to the maximum, does not contain more than about 48 cc., the quantity of air injected cannot have been very great. It will be remembered that Wolf, without serious consequences for the animal, injected as much as 50 cc. at a time; but this, it must be borne in mind, was in one of the main venous trunks, the jugular vein, so that the whole of the 50 cc. was injected into the blood stream. In an antrum puncture, however, the conditions must be quite different. The air does not then make its way into the lumen of a large vein, but is forced into the small veins that are torn away when the mucous membrane is detached from the bone. It is therefore unlikely that any great quantity of air has entered the vascular system. In all prob-

ability only a few air bubbles are forced into the circulation, and it is then a question whether these could cause the alarming symptoms. It will be apparent from the investigations mentioned that small quantities of air in the venous system cannot produce dangerous phenomena. These can only occur when the air passes into the arterial circulation. Jürgensen has proved, however, not only that air in the arterial system passes without difficulty through the lung capillaries, but also that air bubbles in the venous system, at any rate from the vena linealis, may pass into the greater circulation. Wolf himself, who is also an ardent defender of the lung death theory, admits that even the venous air embolus may be carried into the arterial system. He points out that the paralyzes, clonic and spastic contractions, etc., described by Heller, Mager and von Schrötter, really indicate capillary emboli in the systemic circulation.

If these investigations are compared with my two cases in which there have probably been air emboli, it will be seen that it is first and foremost the arterial embolus of which there can here be any question. The symptoms, at any rate, strongly favor this view. Judging from the animal experiments, the venous emboli produce phenomena first of all from the lungs, heavy, irregular respiration. Otherwise the animals showed an astonishing power of resistance to air in great quantities. There is no doubt that the same conditions may also assert themselves in human beings. The following history of a case will be of some interest in this connection.

A pregnant and very anemic woman of about 30, in the State Hospital ear ward, underwent a right sided mastoid operation, with exposure of the sigmoid sinus, the walls of which appeared to be unusually thin and pulsated strongly. After the bandages had been changed several times, about a fortnight after the operation, the patient was to be moved to the maternity hospital on account of her approaching delivery. As no time was to be lost (the pains had already begun), the dressing was done with all possible speed in the ward. Directly the old bandage was removed, a continuous, long drawn, sucking sound was heard, though this was not at once diagnosed as an air embolus. Immediately after, however, the same sound was heard again, and the patient fell to the ground

with loud cries of pain, which was first located over the heart, and directly after over the dorsal surface of the right lung. For a little while the patient was somewhat short of breath, but in a couple of hours was able to be moved to the maternity hospital, where the same day she gave birth to twins and subsequently suffered no inconvenience from her embolus. The sucking of air, in this case, into the sinus only ceased at the moment the patient collapsed. There is no doubt that a considerable quantity of air had been sucked in. The symptoms seem most nearly to resemble Couty's group II. The description of the attack shows that the air could be clinically followed on its way first to the heart and then to the lungs, where its further passage to the systemic circulation seemed to be arrested. It is probable that here the air disappeared from the blood in the following manner. After entering the circulation it is immediately taken up by the hemoglobin, and oxyhemoglobin is formed, whereby the amount of air is reduced 20 per cent. The nitrogen remaining has thus, practically speaking, become pure—that is to say, it has circulated in the blood with a tension of one atmosphere. When this air in the pulmonary veins has begun to mingle by diffusion with air in the pulmonary alveoli, where the tension of the nitrogen is only about four-fifths of an atmosphere, nitrogen is diffused from the air in the veins into the air of the pulmonary alveoli. It will be seen how very widely the features of this case differ from the phenomena that occurred in those of the two antrum patients. In the case of the woman mentioned, there was a large, practically continuous venous air embolus; while in the two antrum patients there was in all probability an arterial air embolus. In the latter cases the small air bubbles must have been able to pass through the lungs and to enter the general circulation, where, by embolizing vital vessels in the central nervous system, they have set up the alarming symptoms.

In reading the history of the cases I have mentioned at the beginning of this work, it will be seen at in addition to my two cases Nos. 1 and 2, air emboli probably also occurred in a number of the other cases described (cf. Claus' Nos. 1 and 4, Neuenborn's, Zarniko's, Fleischer's, Holmgren's and Roll-Hansen's). In most of these cases the bony wall was hard

and difficult to penetrate. The symptoms, moreover, occurred in connection with the injection of air.

The assumption of air emboli is applicable to most cases described, but not to all of them. In my patient No. 3, for instance, the wall of the antrum was thin and the cavity very large. The postmortem showed that no detachment of the mucous membrane had taken place. It will, moreover, be noticed that the dangerous phenomena did not always occur in conjunction with the injection of air, but during the actual syringing (Claus' No. 3 and Henrici's Nos. 1 and 2). In Killian's patient, too, the shock came upon syringing with cold water. If the syringing has been undertaken after a loosening of the mucous membrane inside the antrum wall, it may be likely that also in these cases an air embolus has taken place. Whether, in these patients, it has been an antrum reflex or an air embolus with which we have had to do, can of course never be ascertained; but from my experiments with animals it would appear that the possibility of an antrum reflex ought to be given some consideration. When the question of a nasal "embolus or antrum reflex neurosis" is brought forward, we here enter upon a subject of which very little is told in our special literature, but which, in other medical literature, has been thoroughly worked up in another connection.

It is well known that during the puncture of another cavity, namely, the pleural cavity, alarming phenomena of an uncertain, often mysterious character, now and then occur, and it has not yet been decided whether these are due to air emboli or to a reflex from the pleura.

In connection with this question—antrum reflex or air embolus, it will without doubt be interesting to recall the views that have been put forward with regard to the pleural cavity.

It has long been a well known fact that in affections of the pleura various more or less serious phenomena of an unknown nature may occur, sometimes spontaneously, with great exudation or pneumonias, sometimes in connection with operations on the pleura.

Forlanini classes the symptoms under the heads psychic, motor, circulatory and respiratory. The psychic symptoms manifest themselves in loss of consciousness for long or short periods without lasting effects. The motor symptoms present

themselves partly as spasms, partly as paralyses, often spasms alone, tonic or clonic, which come on simultaneously with the loss of consciousness, and affect most of the muscles. The spasms are often, though not always, one sided. The paralyses are flaccid, monoplegic or hemiplegic. The symptoms from the circulatory and respiratory systems are paretic with small pulse, slightly cyanotic skin and mucous membranes. The respiration is shallow, even ceasing altogether, so that artificial respiration may be necessary. There have also been a number of cases in which operations on the pleura have even resulted in death.

It is needless to say that these accounts published by Forlanini and other well known writers have attracted much attention and have been the subject of considerable discussion in the special literature. A great difference of opinion prevails, however, among both clinical writers and pathologic anatomists, as to the manner in which the phenomena are to be explained. There are especially two views that are of importance. One of these, the embolus theory, which has its warmest adherents among German medical men, maintains that the above mentioned symptoms and death are due to emboli, above all air emboli, resulting from the lesion of the pulmonary veins with the nozzle of the syringe and the injection of nitrogen into the systemic circulation. The negative result of many of the postmortem examinations is not considered to be unfavorable to the theory of air emboli, partly, because the autopsy was not always done with sufficient exactitude, and partly because the air embolus, after inflicting injury, may have been again absorbed.

The other view, the reflex theory, which has gained ground more especially among French and Italian scientists, maintains that the phenomena described by Forlanini and others must be regarded as a pleural reflex, a pleural eclampsia. By this is understood a shock effect produced reflexly from the pleura, and passing either to the circulatory center and the heart, with a heart death, to the respiratory center with disturbance or cessation of respiration, or to the brain with nervous disturbances, loss of consciousness, spasms and paralyses.

As typical attacks have even been brought on by merely introducing the needle into the pleural cavity without injecting

air at all, and as the phenomena are not infrequently transitory, reappearing as soon as the manipulation is repeated, the adherents of the reflex theory are of opinion that emboli cannot be considered probable. As a point in their favor they adduce the frequent entirely negative results of dissection.

One of the writers on this subject, Brauer, takes up an intermediate standpoint. He is of opinion, indeed, that in puncture of the pleura emboli form the commonest complication, and that gas emboli are the natural explanation, especially in the more serious cases; but on the other hand he admits that a reflex from the pleura may occur, although he believes this to be comparatively seldom. He has himself described an undoubted case of pleural reflex arising from the costal pleura. In the case of a patient with pneumothorax who was to be treated for the first time, an attack of suffocation occurred when the cannula came in contact with the exposed costal pleura, a spasm of the glottis, which did not subside until five minutes had elapsed. After an interval of 15 minutes, a light touch with a probe again produced a similar attack. After anesthetizing with novocain, the pleura was punctured with a forcible thrust, a fresh, though less violent attack being brought on. On the other hand, the subsequent treatment with numerous punctures was carried out without complications. It is obvious that there cannot well be any question of air emboli in this case.

The careful study of the literature which Begtrup-Hansen has exhibited in his work on artificial pneumothorax seems to indicate that even serious phenomena which are not always capable of explanation by the embolus theory, may really occur in consequence of even slight pleura manipulations such as an exploratory puncture or the changing of a drainage tube, or merely through touching the pleura. It is sufficiently apparent from the highly instructive controversy between the Swedish doctors, Professor Carl Sundberg and Dr. Em. Lindhagen, on the subject of Sundberg's paper on the cause of the sudden deaths under the pneumothorax treatment, that in the individual cases it will often be extremely difficult, not to say impossible, to decide definitely the question "embolus or reflex." The instructive articles are well calculated to convince

the reader of the difficulty there may be in answering the question in any one given case.

It is obvious that the conditions that apply to the pleura do not permit of being transferred without more ado to the maxillary antrum. The views that are urged for and against a pleura reflex on the one hand and an air embolus on the other, are nevertheless of some interest to us and must therefore not be passed over in a discussion such as this.

Just as there may be difficulty in explaining definitely the symptoms that may appear in connection with a thoracocentesis, so will it be impossible in each separate case to give a satisfactory explanation of the phenomena that are described after an antrum puncture. Nor has this been the primary aim of this work. The main object has been to give an account of the factors that have to be taken into consideration in an antrum puncture, and to direct attention to conditions which, as far as I know, have not been brought forward either in text-books or in our special literature.

As previously pointed out, taken relatively, the serious symptoms appear seldom,* but they are nevertheless of considerable importance from the fact that these phenomena, when they do occur, are fraught with the greatest danger to the life of the patient. We ought therefore to make up our minds that antrum puncture, though apparently such a simple operation, is yet not entirely free from all risk.

The question then is how this risk, which may attend puncture, is, if possible, to be avoided. There are in particular two factors which should be taken into consideration in an antrum puncture. One is the narrow, stenosed ostium maxillare, the other, which is of still greater importance, the thick, firm antrum wall.

If the ostium maxillare, notwithstanding the usual cocaineizing, is stenosed, so that the advance of the air through the ostium is impeded, the opening in the lower meatus, especially in more acute sinusitis with tender mucous membrane, should

*In reality, however, these antrum cases do not appear so rarely as is generally believed. During a discussion on this paper in the Oto-Laryngological Society in Stockholm, several cases were mentioned by Prof. Barany, Dr. Henning, Dr. Sture Berggren and Dr. Ohman.

be made sufficiently large for the air and water to pass through it without too greatly increasing the pressure in the antrum.

If the wall of the lower meatus is so thick and offers such resistance to the insertion of the trocar that the needle can only penetrate the bony wall very gradually, it would perhaps be safest to withdraw the needle, and instead choose the way through the middle meatus. If, for some reason or other, it is nevertheless considered desirable to use the trocar through the lower meatus, the utmost caution should be exercised, as under these conditions it is impossible to be certain that there has been no loosening of the mucous membrane. It might then be better on the whole not to give an injection of air, but on the contrary to endeavor, by aspiration, to make the diagnosis clear, if one does not prefer at once to make a large opening.

In conclusion it is my agreeable duty to offer to Professor S. Torup, head of the Physiological Institute of the Kristiania University, my thanks for his assistance during the preparation of this work.

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I would also take this opportunity of expressing my sincere thanks to Professor Holger Möllgaard, Professor E. Schmiegelow, of Copenhagen, and to Dr. Andreas Janberg, of Kristiania, as also to those of my colleagues who have kindly allowed me to report their cases.

BRANCHES FROM THE MAXILLARY NERVE.

1. Meningeal nerve (middle).
2. Zygomatic nerve.
 - 2 a. Zygomatic facial branch.
 - 2 b. Zygomatic temporal branch.
 - 2 c. Anastomosis between zygomatic temporal branch and lacrimal nerve.
3. Sphenopalatine nerves.
4. Infraorbital nerve.
 - 4 a. Superior posterior alveolar branches.
 - 4 b. Superior middle alveolar branch.
 - 4 c. Superior anterior alveolar branch.
 - 4 d. Superior dental plexus.
 - 4 e. Terminal branches of infraorbital nerve (inferior palpebral, nasal and superior labial branches).
5. Sphenopalatine ganglion.
- 6-9. Branches from sphenopalatine ganglion.
6. Posterior superior nasal branches (median and lateral).
7. Anterior palatine nerve.
 - 7 a. Posterior inferior nasal branches.
8. Median palatine nerve.
9. Posterior palatine nerve.
10. Nerve of the pterygoid (Vidian) canal (great superficial petrosal nerve and deep petrosal nerve).

BRANCHES FROM OPHTHALMIC NERVE.

11. Nasociliary nerves.
12. Frontal nerve.
13. Lacrimal nerve.
 - 13 a. Terminal branches of lacrimal nerve.
14. Spinal tract of trigeminal nerve
15. Nucleus of spinal tract of trigeminal nerve
16. Quintothalamic tract.
17. Gray reticular substance (respiratory center in medulla oblongata).
18. Nucleus of facial nerve.
19. Root fibers of facial nerve.
- 20, 21. Descending tracts issuing from the respiratory center and ending round the nuclei of the phrenic and intercostal nerves in the spinal medulla.
22. Phrenic nerve, motor root fibers.
23. Motor root fibers of intercostal nerves.

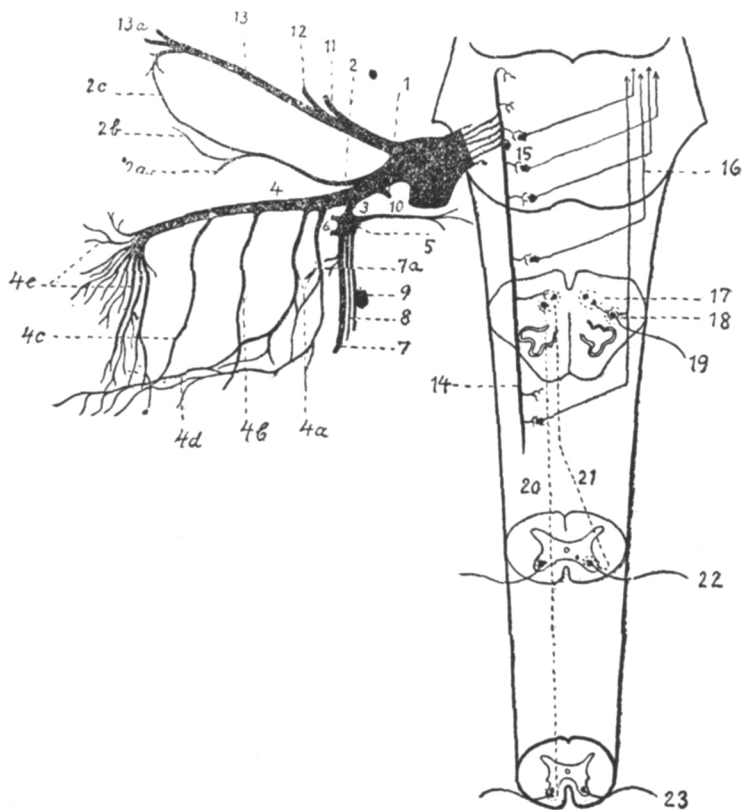


FIGURE I.

Diagram of the peripheral branches from the maxillary nerve, the central trigeminal tracts and their connections with the respiratory center and the facial nucleus.

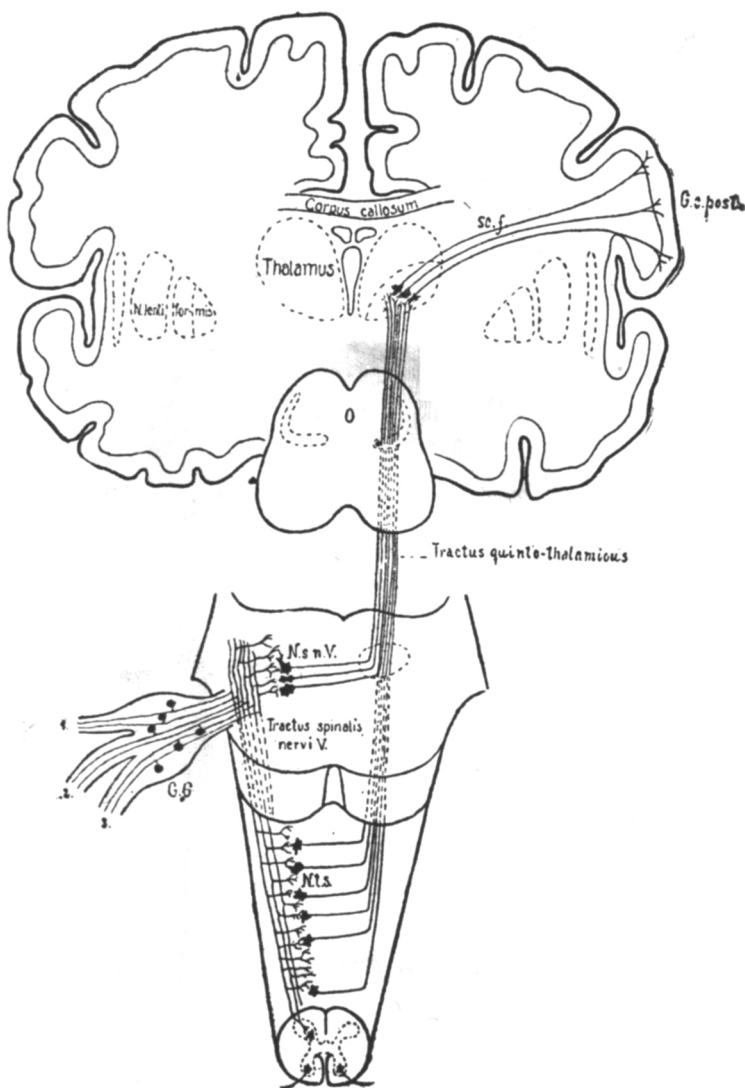


FIGURE 11.

The central trigeminal tracts (from Bechterew). 1, 2, 3, = the 1st, 2nd and 3rd branches of the trigeminal; G. G. = Gasserian ganglion; G. c. post. = posterior central gyrus; N. s. n. V. = sensory nucleus of the trigeminal nerve; N. t. s. = nucleus of the spinal tract of the trigeminal nerve; sc. f. = subcortical fibers from the thalamus to the lower part of the posterior central gyrus.

On the left of the drawing a connection between the descending trigeminal root and the respiratory center is indicated. On the right there is an indication of the connection between the respiratory center and the nucleus of the facial, and further the way in which collaterals run from the fibers in the quintothalamic tract to the cells in the nucleus of the facial.

BIBLIOGRAPHY.

Claus, Hans: Vier üble Zufälle, darunter zwei mit tödlichem Ausgange, bei der Punktion der Oberkieferhöhle. Beitr. z. Anatomie, Physiologie, Pathologie und Therapie des Ohres, der Nase und des Halses. Bd. IV, H. 1 & 2, 1920.

Hajek, M.: Pathologie und Therapie der entzündlichen Erkrankungen der Nebenhöhlen der Nase. Vienna, 1903.

Neuenborn: Ueber einen Fall schwerster Kokainvergiftung. Münchener Med. Wochenschr., 1907, II.

Killian, G.: Ueber üble Zufälle bei Kieferhöhlenausspülungen. Verhandlungen des Vereins Deutscher Laryngologen, 1913.

———: Zur Lehre von den nasalen Reflexneurosen. Deutsche med. Wochenschr., 1910, No. 40.

Zarniko, C.: Die Krankheiten der Nase und des Nasenrachens. Berlin, 1905.

Holmgren, Gunnar: Om de s. k. nasala reflexneuroserna. Hygiea. 1904.

Kjelman, T.: Epileptiforme Anfälle, durch Veränderungen in den Nasenhöhlen hervorgerufen. Berl. kl. Wochenschr., 1894, No. 13.

Jurasz, A.: Die nasalen Reflexneurosen. Heymann's Handbuch der Rhinologie und Laryngologie, Vienna, 1900.

Lazarus, Julius: Ueber Reflexe von der Nasenschleimhaut auf die Bronchiallumina. Arch. f. Physiologie, 1891.

Dixon, W. E., and Brodie, T. G.: Contributions to the Physiology of the Lungs. Journal of Physiology, Vol. XXIX, 1903.

Wolf, Ludwig: Experimentelle Studien über Luftembolie. Virchow's Arch. f. Path., Anatomie u. Physiologie, Bd. 174, 1903.

Jürgensen, Theodor: Luft im Blute. Deutsche Arch. f. Klinische Medicin., Bd. 31, 1882.

Möllgaard, Holger: Studier over det respiratoriske nervesystem hos hvirveldyrene. Kgl. dansk vidensk. Selsk. skrifter, 1910.

Kratschmer, F.: Ueber Reflexe von der Nasenschleimhaut auf Athmung und Kreislauf. Sitzungsberichte d. Wien. Akad. d. Wiss. Bd. 62, 1870.

Sandmann, G.: Zur Physiologie der Bronchialmuskulatur. Arch. f. Physiologie, 1890.

Knoll, Philipp: Beiträge zur Lehre von der Athmungsinervation. Sitzungsberichte d. Wien Akad. d. Wiss. Bd. 92, 1885.

Schmiegelow, E.: Asthma særlig med hensyn till dens forhold till næsesygdomme. Copenhagen, 1889.