

NITROUS OXID AND OXYGEN IN DENTAL
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Since the discovery of chloroform and ether post-operative pneumonia, renal complications and other deleterious results, as well as the danger of death from their use, have baffled the medical fraternity, and the only apparent escape from this condition seems to be through the widespread use of nitrous oxid and oxygen.

The dentist has been so prominent in the discovery of anesthesia and has made his work so well known that this paper shall deal mostly with the surgical field. It is well to state, however, that the nasal administration of nitrous oxid combined with pure oxygen is surpassing all previous results in dental anesthesia.

Recent clinical experiments prove, beyond doubt, that this anesthetic is of great value to the surgeon and a boon to suffering humanity. The premonitory signs of danger produced by nitrous oxid and oxygen are so marked that the patient is much safer in the hands of an inexperienced operator than if chloroform or ether is used, to the extent that the respiration and not the heart is mainly involved, the latter continuing in its normal rhythm some minutes after muscles of respiration are completely paralyzed.

Contraindications for the use of this anesthetic are atheromatous and arteriosclerotic conditions, although I firmly believe that by double diligence with pure oxygen even patients with these conditions may be safely anesthetized. Experiments are under way at the present time by one of our leading surgeons for the purpose of testing the blood pressure with this anesthetic and the safety of its use. Inasmuch as he is substituting common air for pure oxygen, his report will not be conclusive.

Asphyxial symptoms always warn the anesthetist, however, giving abundance of time for the application of simple means for resuscitation, namely, rhythmic traction on the tongue, douching the face with cold water, pulling the chin upward, uniform pressure on the chest, and, in cases of complete suspension of respiration, weak ammonia held to nostrils, etc. Hypodermic injections of strychnin and brandy or ether do no good; the same is true of amyl nitrite, and time should not be wasted trying these restoratives.

Let it be understood that death may follow nitrous oxid anesthesia when the gas is too freely administered, especially when not combined with pure oxygen. It seems to be the consensus of opinion of the medical profession that the time has arrived for the employment of the professional anesthetist, with whom the legal responsibility of death must rest instead of with the surgeon. Hospital staffs and operators are complaining of the loss of their anesthetists whom they have carefully trained. These men remain but a short time in our hospitals, on account of lack of remuneration, and engage in more lucrative practice.

It is generally conceded that there is no medical subject more grossly misrepresented than the concomitant effects of anesthesia. These effects are usually attributed to a thousand and one ills, and while they have been regretted by the surgeon, he has hitherto seen no avenue of escape.

Both primary and remote mortality of chloroform and ether admonish the surgeon to look for a substitute, which seems to have been found in nitrous oxid and oxygen, though the value of this substitute is not fully comprehended by the profession.

Experience shows that the much dreaded cyanosis is due to the lack of oxygen and not to any specific poisonous effects of the gas.

Regarding the danger of death, it is an established fact that the only cases on record of death from the administration of nitrous oxid were occasioned by the administration of this gas alone, and that death has never occurred when nitrous oxid combined with pure oxygen has been administered. Kolischer also quotes the statistics of Bellamy, who reports 4,000,000 administrations in England in four years. It is further stated that seventy-five thousand patients undergo this anesthesia in America annually.

Dr. Gustav Kolischer, a recent and ardent advocate of the use of nitrous oxid and oxygen in major surgery, quotes Israel, who says that 75 per cent of all the deaths occurring in his kidney work are heart deaths. "A perusal of the statistics of trustworthy surgeons shows that the great majority of their deaths in prostatectomies occur in the first forty-eight hours. Nothing is more feared by laparotomists than the paralysis of the bowels due to general anesthesia and the suspension of the activity of the kidneys."

Complex apparatus and trained anesthetists have failed to lessen the deleterious influences of anesthetics on the heart, excretory organs and general vitality, or to alter the total results.

Yet literature, up to the present time, attributes none of these results to nitrous oxid and oxygen; and this statement coincides with reports of such American surgeons as Kolischer, Beck, Bevan, Baccus, Andrews and Lobdell. Our own specialists, like Teter, Thomas and Schamberg, concur in this report. I have during eighteen years performed approximately thirty thousand administrations without a single accident, and at least one hundred of these administrations were for major operations. One office in Philadelphia reports nearly three hundred thousand administrations without an accident.

The anesthetic power of nitrous oxid and oxygen has never been doubted, but the cyanotic conditions arising from its use prevented its adoption to any great extent until, of late, pure oxygen has been the necessary adjunct to place it foremost in anesthetics.

The most noteworthy advance in the use of nitrous oxid and oxygen, as an anesthetic in major surgery, is due to the admixture of pure oxygen, which has thoroughly changed the plan of administration.

Many experiments like the one which M. Martin reports have been tried. He kept a dog in a chamber for three consecutive days, giving it nitrous oxid and 15 per cent. oxygen, after which it regained its normal faculties.

Sprouting seeds fail to grow when placed in nitrous oxid, but resume their growth when pure oxygen is added. Let it be understood that atmospheric air is not a satisfactory substitute for oxygen, especially vitiated air of the crowded surgery room, and that cyanotic conditions may be overcome eight times quicker with pure oxygen.

It is impossible to state definitely the percentage of pure oxygen that may be administered to a patient,

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since there are no fixed rules and every patient requires treatment according to that patient's susceptibility to anesthesia. To one patient, 92 years of age, I administered 25 per cent. oxygen at the close of one hour's anesthesia, while other patients are awakened on a 5 to 10 per cent. An experienced anesthetist will quickly supply the needed proportions required by each patient.

It should be remembered that other anesthetics depress, while nitrous oxid and oxygen stimulate, and the heart is the last organ to give up its function. One of the chief barriers to the universal adoption of this, the safest of all anesthetics, and the one chiefly considered by the surgeon, is the expense, which, however, is not prohibitive, as it might seem. The actual expense per hour is approximately \$6 in consumption of gases.

It should be known that the surgeon in many cases is not free from the censure of selfishness when he will not share his fee with the anesthetist in order to permit his patient to escape the primary and secondary effects of general anesthesia. The anesthetist should be well paid and thus encouraged to devote himself to his specialty.

It is important to mention at this time a new apparatus, invented by Dr. Charles K. Teter, of Cleveland, Ohio, which makes it possible to administer definite proportions of nitrous oxid, chloroform or ether, with pure oxygen. I use the apparatus exclusively in my anesthetics, as does the inventor, Dr. Teter. Important among his recent additions is a warming attachment eliminating the refrigeration of cylinders, also permitting the patient to breath warm air.

In obstetric practice this anesthetic is excellent, because we may obtain analgesia and even anesthesia without muscular relaxation or disturbance of the normal course of labor. Uterine contraction is not in the least interrupted by the use of this anesthetic according to the following method: On the approach of labor pains the patient is permitted to inhale three or four breaths, placing her in a state of analgesia; the inhaler is then removed; and the process is repeated as often as necessary. Should it be desired to retard labor, a small percentage of chloroform may be added. Owing to the rapidity of the action of the gas and its rapid elimination it stands foremost as an obstetric adjuvant. I report two cases of directly opposite type:

CASE 1.—Patient was a multipara, aged 40. Her first child had been delivered with instruments, after thirty-six hours' dry labor. The patient had the left ovary and tube removed and extensive adhesions, due to localized peritonitis, broken up. Her general condition was one of muscular atonicity, malnutrition, etc., due to previous years of suffering preceding laparotomy. The patient became pregnant fifteen years after the operation, gained thirty-six pounds during gestation and was restored to normal health.

Anesthesia.—At full term and approach of delivery, preparation was made to use gas and oxygen. The patient was instructed to refrain from calling for the gas during the early stages of labor. When the pains became severe and more frequent, she was permitted to inhale about four breaths and, as numbness was felt, the mask was removed. This was repeated during four hours with gratifying results to the patient. To quote her statement: "Childbirth has no more terrors."

CASE 2.—The patient was a multipara, aged 30, robust, muscular and athletic. The onset of labor indicated rapid birth. The pains came thick and fast with increasing severity.

Anesthesia.—The patient demanded gas from the beginning. A rigid and undilated os required retardation of labor, which could not be obtained with nitrous oxid and oxygen alone, so 6 per cent of chloroform was combined with the gas until dil-

tion was obtained and then the former methods pursued. The patient was delighted, and extolled the method. Labor was normal and the placenta was naturally expelled.

Final deductions from these cases are: 1. There is no danger of postpartum hemorrhage superinduced by the anesthetic. 2. Patients may have abundance of anesthetic to relieve suffering. 3. A safe and reliable anesthetic may be constantly at hand in case of instrumental or abnormal delivery.

I herewith briefly present a few average abstracted cases and reports of surgeons for whom I have administered this anesthetic:

CASE 3.—Patient, male, aged 48. Operation by Drs. L. L. McArthur and L. E. Frankenthal for carcinoma of pancreas with secondary obstruction to common duct and subsequent enlargement of gall bladder. Patient extremely jaundiced. Nitrous oxid and oxygen anesthetic, one hour and thirty minutes. Results ideal. Patient awakened perfectly rational, and conversed five minutes after operation.

CASE 4.—Patient, male, 30 years of age, tanner. Double inguinal hernia, complicated on one side by omental prolapse, which was adherent to sac, due to old injection of phenol into sac for purpose of cure. Anesthetic, nitrous oxid and oxygen, for one hour and twenty minutes: in every respect satisfactory: patient did not resist in the least and came out of anesthetic with hardly any after-effects. He had a slow pulse and vomited once three hours after anesthetic. (March 20, 1908, Dr. Carl Beck.)

CASE 5.—Patient, female, wife of physician. Large internal and external hemorrhoids, cyst of vagina and perineorrhaphy. Nitrous oxid and oxygen anesthetic for about one hour, excellent anesthetic, no after effects except a slight nausea. (March 24, 1908, Dr. Carl Beck.)

CASE 6.—Patient, female, 48 years of age, "came to hospital March 10, 1908, in an extremely anemic condition due to uterine hemorrhages which had continued for six weeks previously. The vaginal hysterectomy, which was performed on March 12, required an anesthetic for nearly two hours, owing to the complications in the case. The patient was awake ten minutes after the operation, with no ill effects from the anesthetic, no vomiting having followed, and kidneys kept on secreting three to eight ounces of urine every three hours without catheterization. The patient has made a splendid recovery. (Dr. Emil Beck.)

CASE 7.—Patient, male, weighing about two hundred pounds, very powerful, alcoholic, on whom an operation for perivesical abscess with plastic work on the urethra had to be performed. Operation very extensive, for perineal and suprapubic cystotomy. Patient took over four hundred gallons of gas and 1 to 5 per cent of oxygen during the operation. Patient awoke in the operating-room five minutes after the anesthetic was stopped, talked rationally, had no bad effects from the anesthetic, and could be fed with a light diet the same day.

"For difficult cases, or those in which kidney complications are feared I believe this anesthetic is preferable to ether, as the patients are always in better condition as soon as they wake up." (Dr. Emil Beck.)

CASE 8.—Patient, male, aged 5. "At age of two years had severe endocarditis without rheumatism or other apparent cause; life despaired of. Mouth breather, with occasional running ears and intermittent deafness. Examination of heart showed evidence of slight left heart enlargement and systolic murmur at apex and another loud one with seat at aortic area. Pulse-average 85, of fair quality with an occasional intermission. Owing to above condition chloroform or ether was contraindicated. Removal of adenoids by means of Löwenberg's forceps introduced by the mouth and straight forceps by the nose. General anesthesia by nitrous oxid and oxygen. Was most satisfactory in every way. May 6, 1908." (Dr. A. M. Corwin.)

CASE 9.—Patient, female, aged 38. "Ovariectomy, appendectomy and Coffey's operation for shortening round ligaments. Patient was anesthetized with nitrous oxid and oxygen, taking 7 to 10 per cent of the latter, with not a particle of cyanosis present. No nausea or disagreeable after-effects. A delay

of one-half minute was occasioned to obtain relaxation when adhesions were broken up from the inflamed uterus. A greater test could not have been made of this anesthetic than in this case, which proved highly satisfactory in the presence of one hundred visiting physicians. The only possible criticism of this anesthetic is the expense." (May 29, 1908, Dr. A. J. Ochsner.)

CASE 10.—Patient, male, aged 35. "An incision was made from the external canthus of one eye, through the eyebrow, across the bridge of the nose, through the opposite eyebrow to the external canthus. A Gigli saw was passed into the incision, through bone and periosteum, sawing through the septum between the two frontal sinuses. This exposed the cavities of the frontal sinuses, which were thoroughly cleansed of their pathologic condition (granulations); the natural opening into the nose was thoroughly established by enlarging, and through the floor of this frontal sinus the interior ethmoid cells were thoroughly broken down and eurented. Nitrous oxid and oxygen was administered by Dr. Ream during the whole time of the operation, which lasted two hours and which was a perfect success as far as anesthesia was concerned, without the least bad after-effects. In fact, the patient was awake before he reached his bed. This patient had two radical operations on his mastoid previously and during each of these two previous operations a great deal of trouble was encountered from the anesthesia, which was both ether and chloroform, the patient having bad after-effects especially." (May 9, 1908, Dr. Joseph C. Beck.)

I report three major operations in which I administered nitrous oxid and oxygen for Dr. Gustav Kolischer during May, 1908:

CASE 11.—Patient, male, aged 30. Tumor of the bladder. Suprapubic operation. Total suture of bladder and skin incision. Duration of operation, fifty-four minutes. Patient returned conscious to bed. Urinated naturally three hours after operation.

CASE 12.—Patient, male, aged 40. Papilloma of the bladder. Suprapubic total suture of the bladder and skin incision. Duration of operation, forty minutes. Urinated naturally three hours after operation. Slight nausea for about five hours.

CASE 13.—Patient, female, 63 years old. Cyst of the left ovary, and cancer of the cervix. Abdominal celiotomy, removal of the cyst and Wertheim's operation for cancer of the uterus. Duration of the operation, sixty-five minutes. Pulse, 88. Patient regained consciousness after twenty-five minutes. No nausea. Took fluid without any discomfort.

CASE 14.—Patient, female, aged 58. Exploratory laparotomy. Suspected uterine sarcoma. Case pronounced inoperable on account of severe growth and extensive adhesions. Patient had severe myocarditis. Was anesthetized with nitrous oxid and oxygen for forty-five minutes without disagreeable symptoms. Marked absence of cyanosis and nausea. Recovery within five minutes. (June, 1908, Dr. E. C. Dudley.)

CASE 15.—Patient, female, aged 60. Vaginal and abdominal hysterectomy. Same anesthetic, lasting one hour and ten minutes. Results ideal. To quote Dr. E. C. Dudley: "This is the best anesthetic I ever saw in such grave cases." This opinion was also concurred in by Dr. C. P. Caldwell.

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DISCUSSION.

DR. C. K. TETER, Cleveland: I have for the last five years devoted my time exclusively to investigations along this line. I have administered this anesthetic over 12,000 times, and over 1,000 of these administrations were for extensive cases of major surgery lasting from a half hour to three hours. So far as my experience goes, the time does not make any difference; you can anesthetize a patient for a half hour or for three hours, if consistent with modern surgery to keep the patient under the influence of an anesthetic that long. How long a patient could breathe nitrous oxid without bad results would depend a great deal on the condition of the patient and the way it was administered. Nitrous oxid and oxygen form undoubtedly the safest anesthetic now known, and it is more free from after-effects than any other. Following its use, no

degenerative changes take place in the system so far as we have yet discovered. I have given it in all stages of degenerative conditions in the system—sugar in the urine and other kidney diseases, and have never yet had complaint that the patient was rendered any worse. It is quickly eliminated from the system.

The administration of nitrous oxid and oxygen for a major operation requires considerable skill. Almost any one can render the patient unconscious so that he will not be cognizant of the pain of minor operations; but to obtain complete relaxation for extensive laparotomies requires an expert. As a rule, when we begin work with surgeons in laparotomy or other extensive work, they require relaxation; but after they get used to this anesthetic and accustomed to a little rigidity and necessarily more or less cyanosis, they put up with these factors on account of the patient being in a better condition, without mixing chloroform or ether with the nitrous oxid. At first surgeons said that the rigidity hampered them, but now they find that rigidity throughout the whole operation helps more than it hinders; when they close the incision they can do it more rapidly than if the muscles were flabby.

The nature of nitrous oxid is such that to derive its anesthetic effect it has to be given practically pure. That is its drawback. If we could use 50 per cent. pure and get the desired anesthetic effect, it would be an easy matter to administer it, but we have to use it about 90 per cent. pure, and with 10 per cent. only of air, respiration is rendered difficult. For this reason the combination of oxygen with nitrous oxid gives better results than dependence on air. In the average case, eight parts of oxygen will overcome the asphyxial effect of the nitrous oxid. If you are depending on the atmosphere to get the eight parts oxygen, it will be necessary to admit about forty parts air and unless your patient is extremely susceptible to the effects of nitrous oxid you will not get surgical anesthesia. By means of the nasal inhaler, the anesthetic being taken through the nose, the mouth is not obstructed, and oral operations can be performed without the addition of chloroform or ether. With a nasal inhaler you can keep your patient under the influence of the anesthetic indefinitely. It is more difficult to use than the face inhaler, but it can be done very nicely so that all oral operations, as extraction of teeth, etc., can be done as a surgeon should do his work. The idea of the dentist giving nitrous oxid and then accomplishing his work in a few seconds, is not a good one, for he can not do it skillfully and can not leave the mouth in the condition in which it should be left. If by means of the nasal inhaler he keeps his patient anesthetized sufficiently long for him to do the work properly, the gums will be left in a good condition, he has time to clean up the whole mouth at one operation, and when the patient comes out from under the influence of the anesthetic he has no recollection of the work. In doing extracting for dentists I seldom use a face-piece, but invariably the nasal inhaler. I want to know that I can take all the time necessary to do the work as it should be done.

DR. FREDERICK B. MOOREHEAD, Chicago: Nitrous oxid is an established means of anesthesia. Prominent surgeons are using it, and gradually are coming to use it more and more. The question as to the safety of nitrous oxid anesthesia has not been decided. Chloroform has been used as a general anesthetic for a great many years, and only within the last three or four years was its real danger discovered—that of the production of diacetic acid and acetone and subsequent fatty changes in the liver and other vital organs, causing death as a secondary result. We do not know what the permanent effect of the two-hour administration of nitrous oxid is going to be on the hemoglobin after a long period of time. The work of greatest importance in this is yet to be done, and that is to determine the relation between nitrous oxid and hemoglobin. For two years I have with two or three others been trying to do that work, but we have found it exceedingly difficult, inasmuch as it requires a great deal of physiologic chemistry, because hemoglobin is a very intricate compound to study; but that is where the work must be done. The administration of nitrous oxid anesthesia, whether we shall use air or oxygen, depends a great deal on the personal equation, a factor we must

always keep in mind in discussing every subject. I can not take the position that a man can not give nitrous oxid perfectly unless he uses oxygen; no other man can take the position that it can not be administered without air: the administration of this anesthetic depends more on the personal equation than does any other. Our trouble in giving nitrous oxid over a long period of time has been in the fact that we have asphyxiated our patients and not anesthetized them. Its absorption is necessarily slow, and where that critical contact between hemoglobin and nitrous oxid takes place we have not yet discovered. There is undoubtedly an absorption of nitrous oxid into the hemoglobin, this producing the anesthesia. By administering the drug over a long period of time we get anesthesia, and the production of a large amount of carbon dioxid, which is deleterious. We not only get asphyxia, but delirium and toxic conditions following the absorption of a large amount of carbon dioxid. The relation between nitrous oxid and hemoglobin, the nature of the combination and the possible effect on the patient constitute, I believe, the vital question in the whole matter.

The patient will not become cyanotic if gas and air are given in the right proportion. There may be difficulty in producing the anesthesia, however. We can with nitrous oxid and air get anesthesia in the majority of cases without asphyxia, but we have patients with apparently an idiosyncrasy, who, therefore, require more gas to produce anesthesia than is safe to give.

DR. ORVAL J. CUNNINGHAM, Kansas City, Mo.: It appears that nitrous oxid and oxygen anesthesia is as yet in its infancy. We do not know the theory of its dangers, neither do we know the theory of the dangers of chloroform and ether. We know that deaths from nitrous oxid are rare, and that deaths from chloroform and ether, especially chloroform, are comparatively common. In the millions of times that nitrous oxid has been administered there have been reported only about thirty deaths.

The chemical union of nitrous oxid with the hemoglobin—and it seems that such does occur—must be very loose because its action is transitory and when the gas is withdrawn a quick cessation of the symptoms follows. We know that the nitrous oxid is a true anesthetic agent aside from its asphyxial properties. Pure nitrous oxid, nitrous oxid and air, or nitrous oxid with a deficient amount of oxygen, anesthetizes by the combined action of asphyxiation and the anesthetic properties of the nitrous oxid. We can get complete anesthesia in from four to six minutes by simple rebreathing without the use of any anesthetic agent. This asphyxial element of nitrous oxid anesthesia is easily overcome by the proper use of oxygen, but not with air. The cyanosis produced by nitrous oxid with deficient oxygenation, however, is very different from the cyanosis produced by the action of chloroform and ether, except when the cyanosis of chloroform and ether is from obstructed respiration. The cyanosis of nitrous oxid is from a lack of opportunity for the blood to take up the normal amount of oxygen, is not from an abnormal condition of the nervous or circulatory systems, and is no more dangerous than the cyanosis caused by a paroxysm of pertussis. The cyanosis of chloroform and ether is caused by capillary stasis, which is brought about by atony of the capillary vessels or by impaired heart action. The cyanosis of nitrous oxid comes quickly and disappears quickly when oxygen is added; the cyanosis of chloroform and ether comes on slowly, is preceded by an interval of ashy pallor, and disappears slowly, even though pure oxygen is given. Nitrous oxid and oxygen anesthesia is hardly practical for laparotomies in severe cases, because of abdominal rigidity. For other surgical work it is eminently practical if properly administered.

I believe that attention has not been called heretofore to the action of nitrous oxid and oxygen followed by ether, as in the use of Clover, Bennett and other apparatus. With them it is necessary to discontinue the gas at the end of a minute and a half to two minutes because of the asphyxiation which would otherwise follow. This necessitates pushing the ether, and also the use of rebreathing to prevent the patient from coming out. But even then the patient will almost invariably come out enough to swallow about as much as if ether had been

given alone. But if oxygen be added to the nitrous oxid, complete nitrous oxid anesthesia can then be continued until ether narcosis is thoroughly established. By this means we prevent a return of the reflexes between the gas and ether which eliminates the greatest factor in the production of post-operative nausea and vomiting, viz., the swallowing of the ether-laden secretions of the mouth.

THE NON-RELATIONSHIP OF ACTIVE CELLULAR DIVISION TO THE PROGNOSIS IN MALIGNANT DISEASE.*

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There appears to be a wide-spread opinion that the progress of a given case of malignant disease can be foretold by means of a microscopic examination of a portion of the tumor. In other words, it is believed that the number of actively dividing cells found in the tissue bears a definite relation to the rapidity of the growth of the neoplasm. The greater the number of actively dividing cells, according to this opinion, the more rapid the formation of new tissue and consequently the graver prognosis.

In various text-books, in monographs, in pathologic reports, and by direct word of mouth is the above thought passed on from one to another.

Attention was first drawn to this subject by the fact that the majority of squamous epitheliomata contain many mitotic cells. As is well known, this form of carcinoma is not as a rule as malignant in its course as are the other varieties. It was found that in a large percentage of these cases there were many mitotic figures, although the clinical history was that of a slowly growing neoplasm. This being the case, it was thought well to investigate, as thoroughly as possible, the question of the relationship, if any, between the presence of actively dividing cells and the seriousness of the lesion.

In the estimation of the activity of the cells no very accurate method could be devised. Those cells whose nuclei were not broken down and which stained intensely were taken into consideration as well as those in which actual mitotic figures could be observed. The fact that the nuclei remained unbroken and stained very deeply was considered as an indication of the presence of a large amount of chromatin such as is found in actively dividing cells.

The question as to the number present was also a difficult one to answer and had to be done in a purely personal and arbitrary way. It was not difficult to separate the "very many" from the "very few" but it was at times hard to decide when the "many" point had been reached. If several fields of the microscope had to be examined before active cells could be found that specimen would be considered as having few. If every field had several it was then said to belong to the type having many dividing cells.

After taking up the percentage of specimens containing many and few mitotic cells their relation to the duration and to the rapidity of the growth was considered. These figures are open to criticism on certain grounds, particularly when the rapidity is examined into. In many of the cases there is a history of the growth having been present for a number of years, during the greater part of which time it has

*From the Laboratory of the St. Louis Skin and Cancer Hospital.