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MALIGNANT DISEASE OF THE LARYNX AND PHARYNX.

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Introduction.

DURING recent years the treatment of cancer of the larynx and pharynx has received considerable and well-deserved attention. The improvement in surgical technique has increased the chances of success in this specialist branch, and the work of Gluck and Soerensen, St. Clair Thomson and Colledge, Wilfred Trotter, and others has extended and reinforced the foundations well laid by Butlin and Semon towards the close of the last century. Their results enable us to state with some certainty that this cancer can be excised, that that cancer is to be removed only by an exceedingly extensive operation, and that the other is in no way amenable to surgical methods. They also noted that the greater number of tumours of the larynx and pharynx fell into one of the last two categories.

Such cases, most of them in an advanced condition, were referred to the radiotherapists, all of whom did their best according to their lights to alleviate the distressing condition without, however, attempting to correlate their results, which were for the most part not encouraging. Out of this period grew a number of different methods of radiotherapy. In 1920 the Paris school of radiotherapeutists, headed by Regaud, stated certain new principles in the radiation therapy treatment of malignant disease in this situation. A technique was

established by Coutard that yielded better results than any hitherto obtained. Since 1929 it has been practised at Zürich under the leadership of Professor Schinz. The methods and results of this treatment are the subject of this paper.

The region that is under discussion calls for some observations that are important both for the radiologist and the surgeon. Its boundaries are fixed by the roof of the epipharynx, by the choanae and anterior pillars of the fauces, by the posterior wall of the pharynx, by the glottis and the mouth of the œsophagus. The physiological boundary between meso- and hypopharynx, the pharyngo-epiglottic folds, will be accepted as more suitable than the customary anatomical boundaries, which are otherwise satisfactory for our purpose.

The lymphatic drainage is exceedingly rich; the lymph-nodes are numerous and intimately connected; the metastases are common and extensive. The cartilaginous investment is extensive and is very liable to invasion by the tumour, with consequent necrosis. The fragility of the perichondrium encourages such invasion and, should œdema of the hypopharynx or larynx follow, the margin of safety is very narrow before occlusion of the larynx occurs. Infection of the tumour is the rule and the inflammation gives rise to severe difficulties in swallowing.

The upper air passages are lined for the greater part with pavement-celled epithelium. In the upper part of the epipharynx and in parts of the larynx a ciliated columnar celled epithelium is found, while the vocal cords themselves show once more a pavement-celled epithelium. The transition between the two is gradual and the transitional points vary greatly from individual to individual. Further islets of pavement-celled epithelium are to be found in areas otherwise covered with a columnar epithelium. This accounts for the observation that the vast majority of malignant growths in the nose and throat are squamous-celled epitheliomata (German: Pflasterzellcarcinom).

In this area both sarcomata and carcinomata are found. Of the former class, smaller in number, many varieties are found, sarcomata of the lymphoid series occurring relatively more frequently. The malignant growths of the epithelial type are more numerous. They vary greatly in their radiosensitivity. These variations correspond to a considerable extent to their structure. The relations established by Lacassagne and Duval in 1922 form the foundation of the following system of

radiobiology. A carcinoma tends to imitate its mother-tissue. The imitation may vary from that of the closest resemblance through all grades to one in which a likeness is scarcely to be seen. The series of mammary carcinomata provide a very perfect demonstration of such a series. In the case of cancer arising from pavement epithelium, the differentiation may produce either an epithelioma of skin type, with hornification and prickle-cells, or an epithelioma of the mucous-membrane type may appear with its characteristic cells (Holundermarkzellen) and central necrosis. Illustrations 1, 2, 3 and 4* show fully developed epitheliomata of this type. The details appear in each case in the legend.

Such fully differentiated epitheliomata were designated by Lacassagne as "epidermoid." A considerable number of such growths do not show such extensive differentiation. An epithelioma showing here and there the first signs of hornification, a mixture between skin and mucous type, are placed in this group and termed "semi-epidermoid." Two examples of this form of growth are found in Illustrations 5 and 6.

The final stage in this regression is spelled by the "anepidermoid" epitheliomata. Besides the merely completely undifferentiated form this group contains also those two peculiar tumours, the transitional celled carcinoma (Cutler) and the lymphoepithelial carcinoma (Regaud, Schmincke). Examples of these tumours are shown in Illustrations 7 and 8.

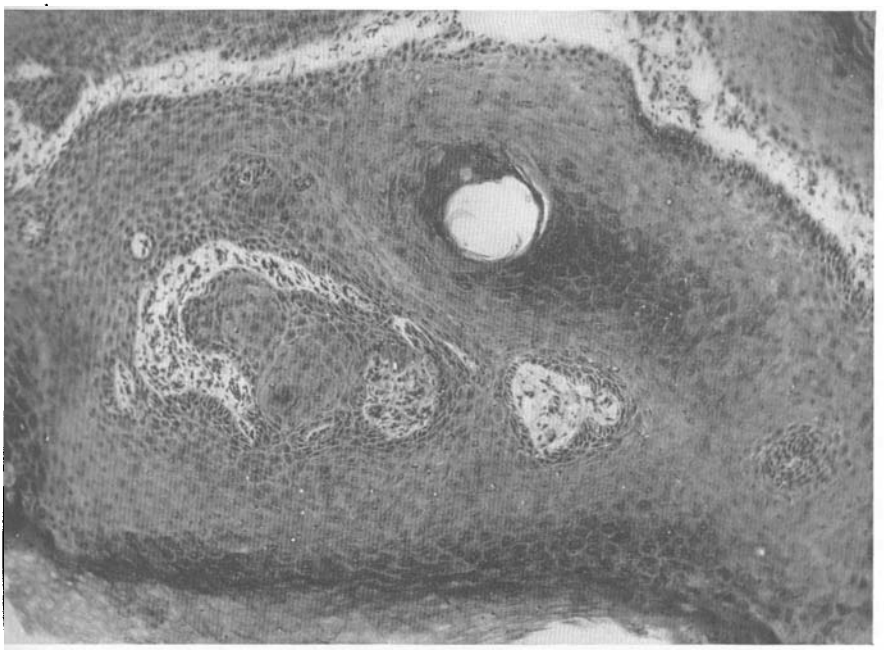
The radiosensitivity of a tumour depends on its place of origin and upon its histological nature. All the epitheliomata of the upper air passages are moderately sensitive. Within these limits the variations are quite considerable and are of great import in the treatment and prognosis. The histological classification outlined above enables conclusions to be drawn as to the sensitivity in any particular case, employing the general principle that the sensitivity decreases with the differentiation. On the other hand, irregularities are often found; thus the anepidermoid epitheliomata characterised by mucous formation within the cell is exceptionally resistant. Similarly, fully differentiated epitheliomata of the skin type, showing certain types of architecture, are much more sensitive than would be expected. Besides the architecture and general histological structure of the tumour other factors, such as the extent of the

* The photomicrographs are from Zuppinger, *Maligne Pharynx- und Larynxtumoren*, 1931, by the courtesy of the author. (Publishers: Georg Thieme, Leipzig.)

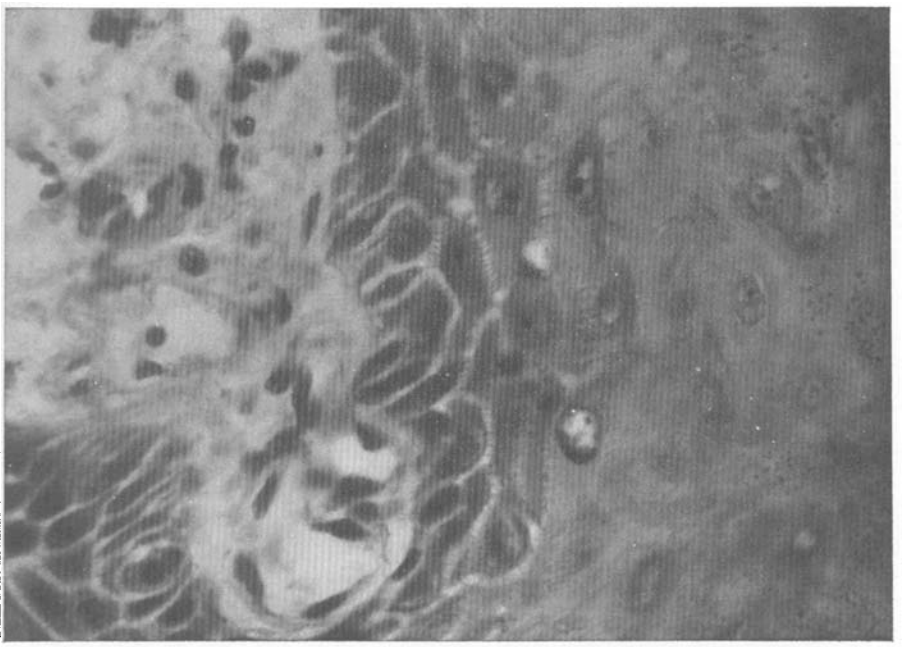
basal cell layer, and in addition the situation of the tumour (not as yet precisely determined), must be taken into consideration in estimating the radiosensitivity of the growth. It is not possible to enter into the details and reference is made to the original works. It must be confessed that the estimation of sensitivity must, in the last instance, be a "feeling" based on the examination of a large number of cases and observation upon their reaction to radiation. The histology is none the less important, as is to be seen from Table I (*vide infra*), which shows the dose required in 13 cases, all of which are at least free from symptoms for eighteen months. On these grounds we perform a biopsy in every case in which the mucous membrane covering the tumour is not intact.

The biological effect of short-wave radiation is purely cytocide—the extent of the effect varies directly with the sensitivity of the cell, which varies from tissue to tissue. Cancer cells are sensitive. Very slightly less sensitive are the cells of the epithelium from which it springs, while the essential tissues (in particular the sub-epithelial blood vessels) are usually somewhat more resistant. These relations exhibit constancy neither from individual to individual nor from tissue to tissue in the same individual. It is not, therefore, possible to speak of a *carcinoma dose*, by which is meant a dose that will kill the cancer cells and do no irreparable damage to normal, essential structures. The possibility of increasing the sensitivity of the tumour or of decreasing that of the other tissues has, since the beginning of radiotherapy, received much attention. In the opinion of Wintz cancer tissue recovered from the effects of radiation quicker than the normal tissues, and he therefore advanced the view of the *highest possible dose in the shortest possible time.*

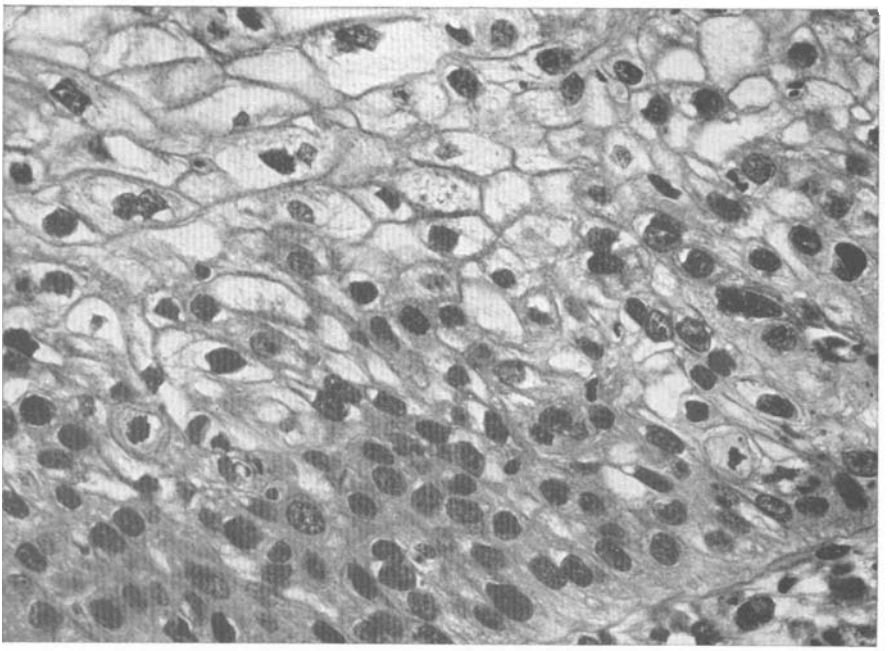
Regaud, in 1922, with radium and, later, Schinz and Slotopolsky (1925) with X-rays showed, however, that in the particular case of the testis (ram and rabbit) it was not possible to induce a radiation azoospermia with one dose without at the same time causing extensive and irreparable damage to normal tissues (skin, blood vessels). On the other hand, by lengthening the duration of treatment, the desired result was obtained with a smaller total dose and *the normal tissues would not be permanently damaged.* Two factors are probably concerned in this result. Firstly, it appears that the essential tissues, especially the blood vessels, recover more rapidly than spermagenetic cells. The second factor is more theoretical. The



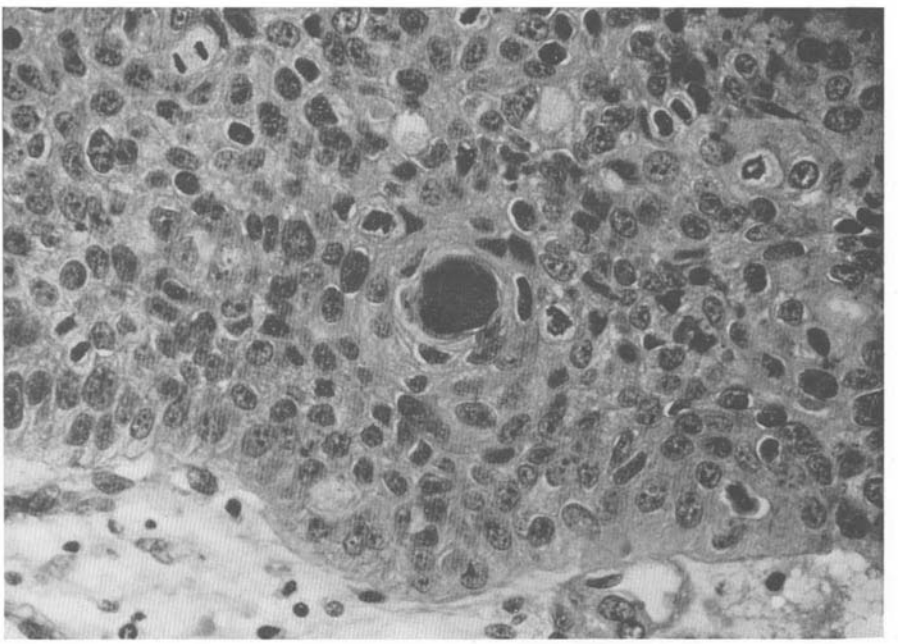
ILLUS. 1.—Epithelioma, epidermoid, skin type. Differentiation is complete. The cell nests show the characteristics of the skin epithelium. The basal cell layer is clearly defined and, in the centre, hornification is perfect. Almost all of the hornified cells have lost their nuclei. Occasionally single horny cells are to be seen. By this magnification the prickle cells are not to be seen. × 92.



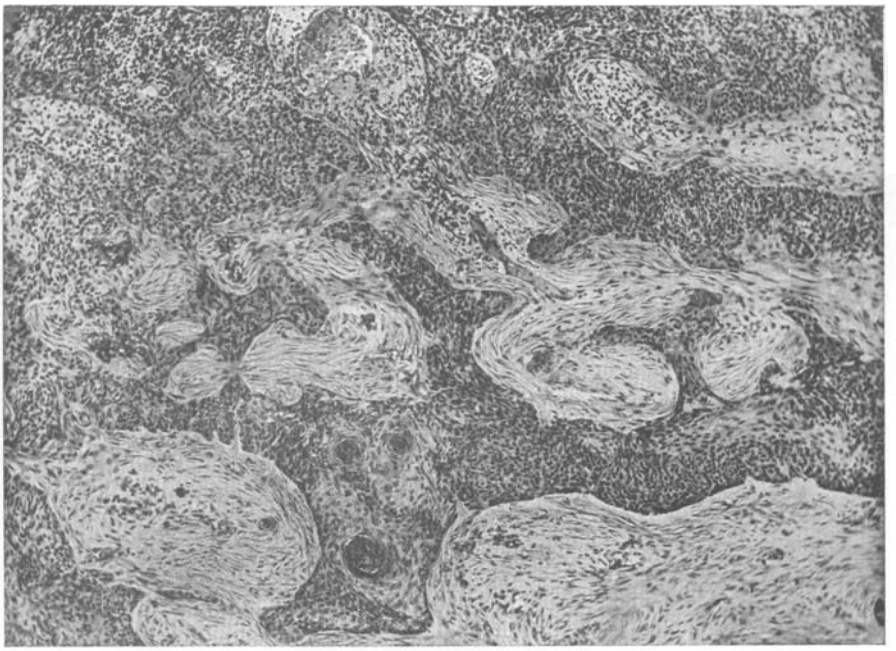
ILLUS. 2.—The same as Illus. 1, higher magnification. The prickle cells are clearly to be seen. Hornification in single cells. × 420.



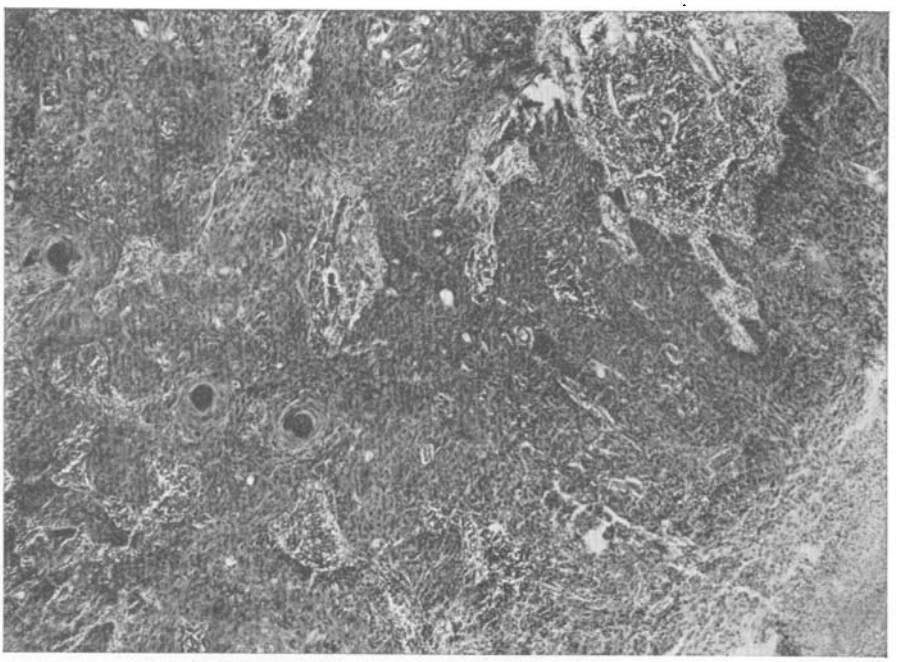
ILLUS. 3.—Epithelioma, epidermoid, of mucous type. Differentiation is complete. Large polyhedral cells, suggestive of the squamous cells of epithelium are seen. In many cases the cytoplasm is very faint, giving the cells a vacuolated appearance (Hollundermarkzellen). Some cells have lost their nuclei but do not show hornification; on the contrary, necrosis of such cells is to be seen. No prickle cells are to be found. × 420.



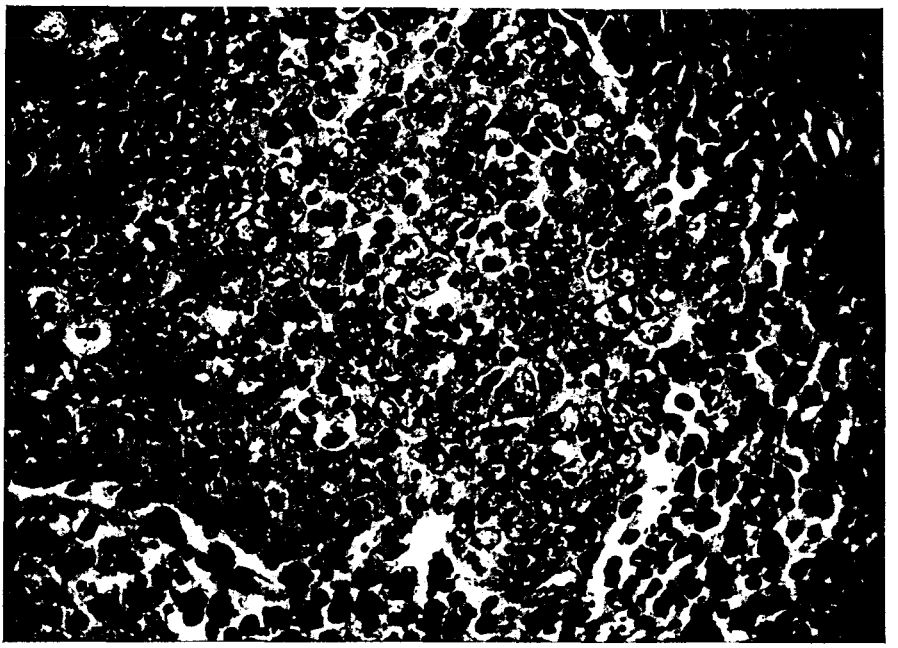
ILLUS. 4.—Epithelioma, epidermoid, of mucous type. Shows the "cell nest" found in epitheliomata of this category. At the periphery are seen the Hollundermarkzellen. In the centre the cells are crowded together but retain their nuclei. The final stage of such differentiation is a central necrosis. × 420.



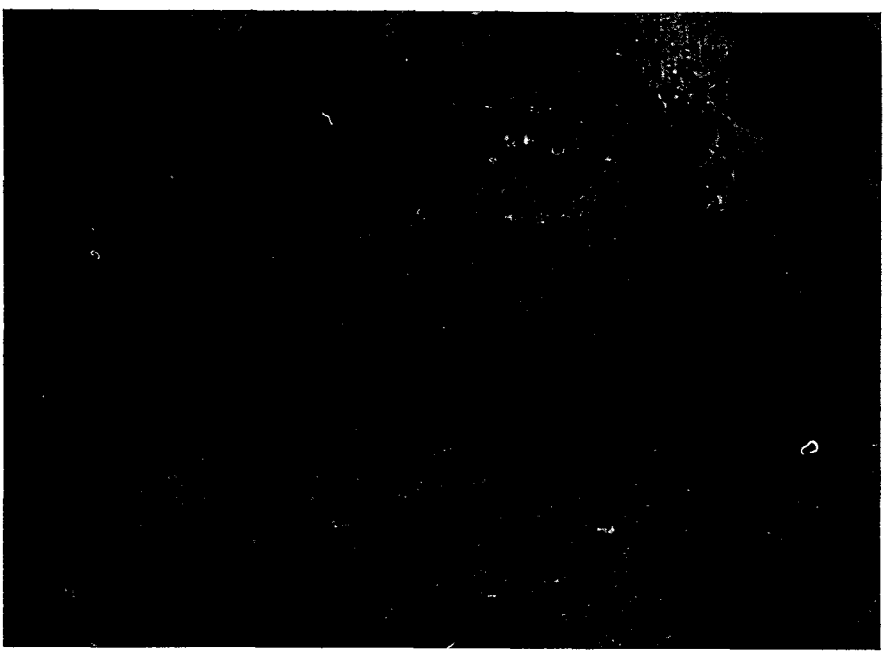
Illus. 5.—Epithelioma, semi-epidermoid type. Differentiation is incomplete. In the majority of the malignant strands the cells are not stratified and the cells show neither vacuolation nor prickle formation and hornification. Occasional incomplete horn pearls are to be seen; the cells have not lost their nuclei. Such differentiation as is present is of the skin type. × 49.



Illus. 6.—Epithelioma, semi-epidermoid type. The differentiation is incomplete; occasionally cell nests of the mucous type are seen. Neither necrosis nor Hollundermarkzellen are present. Differentiation tends towards an epithelioma of the mucous type. × 49.



ILLUS. 7.—An epidermoid, lymphoepithelial carcinoma. The tumour grows in such situations, where epithelium and lymph tissue are in intimate association, *e.g.*, tonsil, nasopharynx. The cells are of the two corresponding types. The cells of epithelial type grow in irregular rows and show no signs of differentiation. The individual cells are large and not sharply defined. The tissue is thickly infiltrated with small basophilic cells of the lymphoid type. × 420.



ILLUS. 8.—An epidermoid carcinoma. Transitional cell. This tumour has a strong familial and biological resemblance to the lymphoepithelial tumour. The lymphoid infiltration is, however, absent. The cells are large, pale and badly differentiated. The tumour grows in broad strands, in the centre of which necrosis is to be seen. × 138.

spermatogenetic tissue exhibits in enhanced form a process that is shown by all living tissue. Some of the cells always, and all of the cells at some time, can be found in reproduction. Schinz observed that although very high or, alternatively, fractionated doses were necessary to induce permanent azoospermia, much smaller doses sufficed to cause a temporary azoospermia. Such a result confirms the suggestion, originating from Regaud and Blanc, 1906, that a small dose permanently kills the cells undergoing mitosis, either leaving intact or but temporarily damaging those that are in a resting stage, and which are destroyed only by much higher doses. The effect of repeating the small dose is to catch these latter cells in their sensitive stage. In 1923 Schinz and Nather in experiments on mice showed that tissue was, in general, most sensitive to short-wave radiation during the period of growth. The application of these results to the radiobiology of malignant growths is but a short step and allows the following conclusions:—

By lengthening the time (decreasing the intensity) of irradiation, by decreasing the size and increasing the number of the single doses it is possible to obtain a differential effect between essential and malignant tissues, by which the malignant tissues will be more effectively destroyed and the healthy tissue will suffer no irreparable damage.

The protraction must not be carried to such lengths that the malignant cells themselves have time to recover and so develop the phenomenon of radiation immunity. The optimum exists and appears to correspond to an irradiation with the following technique.

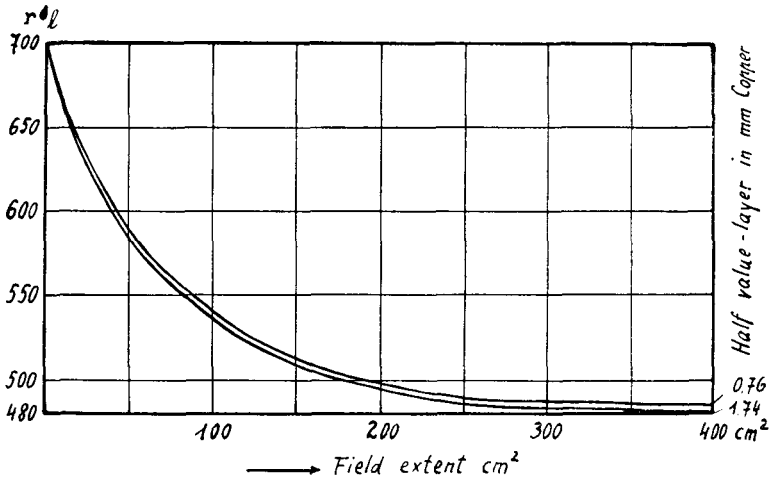
Technique.

Observing the principles expressed above, Coutard developed and improved a radiation technique which showed a much greater success than any other form of X-ray therapy, particularly in the treatment of cancer of the larynx and pharynx. He reported on the method in 1928 to the Second International Congress of Radiology, and since that time the method has been studied and used in the University Röntgen Institute, Zürich, under the direction of Professor H. R. Schinz and his assistant, Dr. A. Zuppinger, who designate the method as "Protracted-fractional Irradiation" (Synonyms: Coutard-therapy, Langzeitbestrahlung, Dauerbestrahlung, etc.).

In this institute a Stabilivolt transformer, Müller tubes,

a tube tension of at least 170 kilovolts and a tube current of 3 milliampères are employed. The radiation is filtered through 1 mm. aluminium + 1·3 mm. copper and the resultant half-value layer is equivalent to 1·35 mm. copper. The focus-skin distance varies between 65 and 75 cm.: it is adjusted to radiation intensity of 2·5 Röntgens per minute measured in air (r/l per min.), a delivery of 3·6 r/l per minute at a focus-skin distance of 50 cm.

The fields are chosen to include the primary tumour and the area of regional metastases. For all tumours two lateral fields are employed and in the case of tumours of the hypopharynx



ILLUS. 9.—The relation between the size of the field and the close in air required to produce a skin erythema.

and larynx often three. The size of the fields is measured and from the curves of Jacobi and Liechti the intensity of the radiation on the surface (r/o) can be estimated (Illustration 9). For example, for a field size of 200 cm.² 500 r/l will be necessary to produce a skin erythema. For a standard field (48 cm.²) according to our measurements 600 r/l are necessary for a skin erythema. The surface dose is therefore (in this case) 6/5 the dose measured in air. It is the therapeutically important dose and is referred to as r/o.

When no contra-indications are present the patient is irradiated daily on the side of the lesion. On five days in the week one of the other fields is treated in addition. Sunday is still a holiday. With infrequent exceptions 180 r/l are applied

at a single sitting. The treatment usually requires about three weeks for its completion. A protracted-fractional irradiation shows a more or less constant clinical course. About the third day some patients may experience a feeling of malaise, with loss of appetite—symptoms that are amenable to treatment and disappear during the following days. About the same time the "early reaction" that is sometimes met with will appear. The cancer tissue and the surrounding mucous membrane show a slight œdema; the metastases may increase slightly in size, or hitherto impalpable metastases may be demonstrated. Subjectively these signs may be accompanied by radiating pains in the neck. The early reaction is of little importance and only infrequently compels a modification of treatment, in the sense of dose reduction or omission, in the case of tumours of the hypopharynx or larynx when the œdema might convert a partial into an absolute stenosis.

Should the irradiation be continued according to plan there will appear, usually between the twelfth and fourteenth days, with a total dose of about 4000 r/o (the limits of variation are very wide indeed), the first objective sign of the reaction of the mucous membranes (mucous reaction, Radioepithelialitis). The *mucous membrane will appear red and lose its shine. It is* accompanied, or occasionally slightly preceded, by its symptoms, namely, a continually increasing pain in the throat and difficulty in swallowing. Both before and during this period a decrease in the size of the tumour may be observed; it will show surface necrosis; it and the immediate neighbourhood will be covered with a yellow-grey membrane. Shortly afterwards, very delicate yellow white membranes of the fibrinous type will stipple the mucous membranes that lie in the path of radiation. They are usually, but not invariably, first to be observed on the soft palate. The treatment must be continued and the membranes will extend. Still quite delicate, they run together and form a continuous sheet, which gradually becomes thicker, more definitely yellow-grey, and takes on a necrotic character. The epiglottis tip is usually the last structure to show a reaction.

The epithelium of the mucous membrane is destroyed. *This is the only criterion of a sufficient dose.* It is exceedingly important; except in the case of very sensitive tumours it must always be obtained and the margin of safety is small. The appearances are almost alarming and the subjective difficulties of the patient are great; he must be reassured that it will heal almost without or entirely without trace.

Beyond this point the irradiation may not be pushed—the subepithelial tissues would be damaged and healing would not occur. But the absolute necessity of carrying the irradiation to the stage of a severe reaction must be emphasised. Earlier failures in favourable cases were almost without exception due to insufficient dosage.

That the doses necessary for the production of such a reaction vary within quite wide limits is shown by the following table:—

TABLE I.

The Dose required in certain Cases, Symptom-Free from 1½ to 3 Years.

Situation.	Histology.	Dose r/o.	Number of Skin Fields.
Epipharynx . . .	Ca. lympho-epithelial	6870	3
Tonsil	Sa. reticular	5890	3
Base of tongue . .	Ca. epidermoid, mucous type	6020	2
Vallecula . . .	Ca. semi-epidermoid	7030	3
Lateral mesopharynx .	Ca. epidermoid, skin type	6360	3
Aryepiglottic fold . .	,, ,, ,,	8000	4
,, ,, . .	Ca. epidermoid, mucous type	6240	3
Arytenoid . . .	,, ,, ,,	6060	3
Sinus pyriformis . .	,, ,, ,,	4980	3
,, ,, . .	,, ,, ,,	3450	3
,, ,, . .	,, ,, ,,	5300	3
Larynx (intrinsic) .	Ca. epidermoid, skin type	7730	4
,, ,, .	,, ,, ,,	6750	3

In spite of cessation of irradiation with the establishment of the confluent mucous membrane reaction, the latter makes further progress during the next day or two; at least the symptoms will become more severe. After this latent period has passed healing sets in—the necrotic membranes show a sharp boundary with a basal inflammatory reaction of the surrounding healthy mucous membrane. Islets of healthy epithelium appear and the necrotic debris is shed. In a period of six to ten days from the cessation of treatment the mucous membrane will show little trace of the trial that it has undergone. In two weeks the mucous membrane shows but the slightest differences from the normal.

The skin shows changes exactly comparable in principle with those of the mucous membrane. The reaction appears later and lasts longer than that of the mucous membrane. About the twentieth day, that is towards the end of the irradiation, the skin reddens and then turns a smoky reddish-brown, a stage that is usually reached at the same time as the

florid reaction of the mucous membrane. During the course of the next few days the horny layer comes away in scales and flakes and it is usually closely followed by a moist eczematous desquamation of the epidermis or, occasionally, by a dry form of desquamation, the latter usually appearing when, for some reason, the treatment has occupied a longer time than usual.

The moist reaction can be very extensive and the necrotic debris of epidermal cells and sterile pus with occasional traces of blood, necessitates a change of dressing three or four times a day. As in the case of the mucous membrane reaction, no irreparable damage is done. Islets of healthy epithelium appear, and in the course of a fortnight, with the exception of the hair which takes longer, the skin is restored to normal. During these reactions in favourable cases the tumour necroses and at their conclusion is usually no longer to be seen. Sometimes its disappearance can be followed; in others, examination with the laryngeal mirror offers difficulties owing to the subjective symptoms of the patient and the necrotic material that covers the parts. In these cases the examination must be limited to that which is necessary to judge the state of reaction.

The metastases, if any, will also show resorption towards the end of treatment—the change is slow and their disappearance may be delayed for as long as two months.

In our material of three years' standing we have observed no case of remote damage to the tissues as a result of these large doses. Equally Coutard in his ten years' material has no case to report in which remote damage has been caused.

Unfortunately, in a number of cases either the primary lesion or the metastases, or indeed both, will not entirely disappear. Up to two months further resorption is possible. Should a rest-tumour remain after this period, it should be regarded as malignant and the prognosis is, on the whole, unfavourable. It is true that in some cases a rest-tumour has been excised and no malignant cells have been found; on the other hand such cases are rare and any rest-tumour calls for frequent and close examination so that, on the first signs of growth, treatment of a relatively small rest can be undertaken. Large rest-tumours are not amenable to treatment.

The fact that the patient has been once submitted to protracted-fractional radiation does not preclude any particular method of further treatment. Surgery with the knife or diathermy, radium, or a repetition of the X-ray treatment, are all

possible and have been practised. Nevertheless, further treatment calls for very considerable care: further treatment in the radiated area presents more difficulties than in untreated tissues. Successes have been rare. It will suffice here to mention that the growth will not respond well to a second radiological treatment and, unless the rest-tumour is small and accessible to radical surgery, the prognosis is grave. The treatment of rest-tumours is fully described in the works of Zuppinger, to which reference is made.

A special consideration of carcinoma of the tonsil is necessary. We have been struck by the fact that the not uncommon rest-tumour, or recurrence after treatment of these growths, has been found in the angle between the fauces and the tongue. Recently we have been accustomed to wait only until the reaction from X-rays subsides in these cases, and then, whether a rest-tumour remains or not, to carry out a surface application of radium. The combination was originally suggested by Berven and we use his special applicator for the purpose. A dose of about 0·8 mcδ/cm^2 is given in approximately ten daily sittings of about two hours, and towards the end of the treatment a local mucous membrane reaction, very similar in appearance and course to the X-ray reaction, appears in the irradiated area. The cases are too few and too recent to allow final judgment of the results.

The above description of protracted-fractional X-ray treatment can best be illustrated by certain examples, which show the typical treatment and some of its modifications. In all cases the tension, milliampèreage, etc., is kept constant, and unless it is expressly stated to the contrary, the technique of irradiation already described has been observed.

Case I.—F. G., male, 51. Inoperable polymorphic sarcoma of the right tonsil, with homolateral metastases "prognostically" inoperable.

Treatment according to general plan. The principal field on the right side, 370 cm.^{2}, covered the tonsillar area and the whole of the right side of the neck in order to include the supraclavicular glands. It received a dose of 2250 r/o in 10 sittings, each of 180 r/l in 80 minutes. The field on the left side, 230 cm.^{2} in area, received a dose of 1520 r/o in 7 sittings. The total dose was therefore 3770 r/o. On the 4th day of treatment a reduction in size of the tumour and of the metastases was noticed. On the 9th day of treatment the patient complained of pain on swallowing. A few flecks could be seen on the fauces; the tumour could hardly be seen. On the 12th day of

treatment delicate membranes were present and the tumour with its metastases had disappeared and the treatment was concluded. The irradiated skin was depilated and red. Ten days after the conclusion of treatment the mucous reaction had disappeared; the mucous membrane appeared entirely normal. The tumour and its metastases had entirely disappeared; the skin showed a few flakes and scales.

Six weeks later the patient complained once more of difficulties in swallowing and breathing. A reddening and mild œdema of the mucous membrane was to be seen. No sign of tumour or metastases. The skin appeared entirely normal and the hair was beginning to grow. In three weeks the symptoms and signs of this second reaction had disappeared.

With the exception of a slight dryness of the mouth, the patient has since that time been (one year ago) absolutely free from symptoms and signs of disease.

Summary.—A very sensitive growth required a relatively small dose for its disappearance. In spite of this a mild reaction appeared. The patient showed the phenomena of a second reaction and is now free from symptoms for over a year.

Case II.—E. M., male, 62. Inoperable carcinoma, fully developed mucous type, left sinus pyriformis. Regional metastases could not be detected clinically.

The treatment followed a normal course. As metastases could not be found, three fairly small fields were chosen. The main field, left, 90 cm.^{2}, received 3000 r/o in 18 sittings. The median accessory field (50 cm.^{2}) received 610 r/o and the right lateral field (90 cm.^{2}) 1370 r/o. The total dose attained was 4980 r/o and the treatment was complete in twenty-one days. On the 14th day of treatment the patient complained of difficulty in swallowing, on the 16th day the first signs of reaction were to be seen. On the 21st day extensive confluent membranes were found to cover the whole of the lower pharyngeal mucous membrane. At this time the patient could hardly swallow and the treatment was stopped. Owing to the difficulties of examination the tumour could not be observed accurately.

Six days later the necrotic membranes began to disappear: the tumour could not be seen; there was only a certain amount of œdema of the arytenoid region. At this time the skin, hitherto a dark red, began to peel and two days later the eczematous stage developed, large areas of necrotic epithelium being shed. Approximately a fortnight after the cessation of treatment, the laryngeal mirror showed a normal condition, with the exception of a slight œdema of the arytenoid region which peristed for another week. Both the skin and mucous reactions were healed. No tumour could be seen. No further complication developed.

Summary.—A moderately sensitive carcinoma disappeared under the influence of the treatment, which, by a relatively low dosage, produced a satisfactory reaction. The patient is now, two years later, free from all symptoms.

Case III.—G. S., male, 55. Inoperable carcinoma of the arytenoid region. Mucous type, not fully differentiated. Large inoperable gland metastases on the same side.

Standard Treatment: The principal field, on the right side (180 cm.^{2}), received 3890 r/o in 18 sittings. The two accessory fields (130 and 50 cm.^{2}) received, together, 2180 r/o. Total dose, 6070 r/o. On the 13th day the first signs of the reaction of the mucous membranes appeared. The tumour had decreased in size. The metastases showed no change. On the 24th day the reaction was severe. Membranes were seen over the whole of the mucous membrane of the pharynx. The skin was dark red. The glands were very much smaller.

A week later a severe moist skin reaction set in, which healed in seven days. The mucous reaction was already healed. It was now possible to undertake a proper laryngeal examination. Except for a slight œdematous swelling of the right arytenoid region, the conditions were normal. The glands had not disappeared, but were now smaller and movable. After some weeks the patient was persuaded to submit himself to operation and the glands were radically removed. *Microscopically they showed carcinoma cells. The course of the operation was normal and healing not delayed.* Except for a slight but stationary swelling of the right arytenoid the patient has, until now, presented no signs or symptoms of disease.

Summary.—Disappearance of a rather insensitive tumour as a result of irradiation. Successful operative removal of glands that before the irradiation were inoperable. Symptom-free more than two years.

Case IV.—J. H., male, 69. An operable carcinoma of the left vocal cord. Fully developed skin type. No metastases. The necessary hemi-laryngectomy was rejected on account of the patient's age.

Normal course of irradiation. Principal field (90 cm.^{2}): 3860 r/o in 20 sittings. Two subsidiary fields (90 and 50 cm.^{2}) together: 2890 r/o in 16 sittings. The first signs of the mucous reaction did not appear until the 19th day, probably due to the fact that the fields were exceptionally small. The reaction lasted longer than usual, no less than three weeks.

The treatment was concluded on the 23rd day. Eight days later there was a definite moist reaction of the skin, which, however, lasted

only 4 days. During the irradiation the growth became smaller. As soon as accurate examination was again possible, 5 days after cessation of the treatment, no tumour could be seen. Until now the patient has been entirely free from symptoms.

Summary.—Under the influence of the radiation an elderly man was relieved of an operable growth that proved itself moderately sensitive. He is now in full possession of health and voice, very nearly two years after the commencement of treatment.

Case V.—E. W., male, 61. Prognostically inoperable carcinoma of the right sinus pyriformis. Fully differentiated mucous type. Inoperable, hemilateral regional metastases, with a history of more than $2\frac{1}{2}$ years.

Normal technique of irradiation. Principal field (190 cm.^{2}): 3450 r/o in 16 sittings. Two subsidiary fields (150 and 70 cm.^{2}): 2660 r/o in 13 sittings. On the 9th day the patient had difficulty in swallowing and on the 14th day there were reaction membranes in the pharynx. On the 18th day treatment was stopped, but the mucous reaction continued to increase, reaching its zenith two days later. It required a further week to heal entirely. The skin reaction appeared later, nine days after cessation of treatment, and healed in five days. By this time the primary tumour had disappeared and the gland metastases were very much smaller. These latter continued to decrease during the next weeks, and two months after treatment there remained but a vague infiltration where they had been. Six months later no signs of the metastases could be found and the laryngological appearances were normal. The patient has remained free from symptoms, with the exception of a little dryness of the mouth, until the present day.

Summary.—An extensive, moderately sensitive tumour, with extensive metastases, has been free from signs and symptoms for very nearly two years. The metastases disappeared slowly.

X-ray treatment on these lines calls for accurate assessment of the indication in each individual case.

It is true that we have attempted in almost all the cases referred to us to carry out the treatment. In some in which treatment was discontinued it should probably never have been begun. In others the patients, although showing a good local response, developed complications, of which by far the most common has been an aspiration pneumonia, not infrequently fatal. In addition to these problems that develop during any

form of treatment, there are others, quite peculiar to this form of radiation therapy, that call for most anxious attention on the part of the radiologist. The question as to whether the general reaction of the patient calls for the omission of a sitting, whether the speed of appearance of the reaction calls for a modification of the dose, etc., is difficult. Above all, the assessment of the data obtained from the laryngeal mirror in conjunction with the general condition of the patient during the time of the reaction, which factors alone determine the moment for cessation of the treatment, are not easy to decide. Hospitalisation of the patient is *essential* and the radiologist should have every facility for the clinical control of a patient during a treatment that must be considered at least as severe as a major operation.

By accurate dosage we have never observed serious sequelae as a result of protracted-fractional radiation. Necrosis of the jaw may be prevented by rigid attention to the teeth at the beginning of treatment. Cartilage necrosis (larynx, etc.) as a sequela we have not observed, except in two cases which had already been tracheotomised. A partial destruction of the larynx due to invasion of the growth is, however, often to be seen at the beginning of treatment. It may also lie hidden and first manifest itself during the course of the treatment. The prognosis in these cases is very unfavourable, owing to the unavoidable infection. In cases with threatening asphyxia a trial should, if possible, first be made with X-ray treatment. We have been successful in avoiding tracheotomy even in cases which were admitted expressly for tracheotomy. Should the operation be absolutely unavoidable low tracheotomy should if possible be performed, in order that the track of the cannula may not lie in the irradiated area (Zuppinger).

Disturbances of salivary secretion are sometimes met with which cause the patient annoyance. They are often improved by very small doses of physostogmine. The irradiated skin usually recovers its normal appearance after a month or two. Occasionally a permanent brown coloration remains and, in rare cases, unsightly teleangiectases are found. In the latter case it has been due to the further irradiation of a field already showing a severe reaction. In some cases, after an interval of two to four months, a mild secondary reaction appears—redness and perhaps œdematous swelling of the irradiated mucous membranes, a mild subcutaneous œdema and variable subjective difficulties of a trivial nature. In the course of one or two

weeks these troubles disappear again. The difficulties and dangers of the method are relatively slight and with experience should soon be overcome or avoided. The results of the treatment will be demonstrated in the next section.

The Results.

In the following tables the results of this method of treatment from Spring 1929 to the end of 1931 are shown. The total number of cases is 144, and all cases are included that have been referred to us since this form of treatment was commenced.

TABLE II.

	A.	B.	C.	D.	E.	F.	G.	H.
	Total.	Completed Treatment.	Initially Free from Symptoms, Primary and Regional.	Symptom-Free Locally. Distant Metastases.	Recurrence, Primary or Regional Glands.	Symptom-Free. Died of Intercurrent Disease.	Now Symptom-Free, 2 to 3½ Years since Treatment.	Optimal Local Success.
Epipharynx	4	2	2	...	...	...	2	2 : 2
Tonsil	24	19	11	1	4	...	8	9 : 19
Base of the tongue	16	13	6	1	...	2	7	10 : 13
Vallecula	11	10	6	...	4	1	3	4 : 10
Lateral and posterior wall, mesopharynx	4	2	2	...	1	...	2	2 : 2
Epiglottis	4	4	3	1	2	...	...	1 : 4
Aryepiglottic fold	7	7	6	1	1	1	3	5 : 7
Arytenoid	4	4	3	2	...	...	2	4 : 4
Sinus pyriformis	44	38	17	4	...	7	7	18 : 38
Postcricoid	2	1	...	...	1	...	...	0 : 1
Extensive hypopharyngeal growth	9	5	2	...	...	2	...	2 : 5
Intrinsic laryngeal	15	11	7	...	...	1	6	7 : 11

In the subsequent analyses the classification according to localisation will be simplified and the following table used as a base.

Of the 144 cases, the treatment could be carried to a conclusion in 116 (80 per cent.). The cessation of treatment was almost without exception indicated by the bad general condition of the patient, in some cases admittedly aggravated by the therapy. In some the patient declined further treatment. *In no case was the extent of the tumour, or of its local metastases,*

a reason for not attempting the treatment; treatment was occasionally carried out in the presence of distant metastases in an effort to relieve a severe asphyxia. In many cases, more particularly since knowledge of the possibilities has spread, the material has shown with a sorry frequency cases that from the beginning must be regarded as hopeless. We do not, however, feel justified in taking from a patient his one and only chance of a temporary improvement—the case is therefore accepted and treated. In such cases the radiation would not be carried to the extent of a severe reaction. The base figure on which to assess the results is therefore given in column B—concluded treatment. As local successes, are reckoned those cases that are

TABLE III.

	A.	B.	C.	D.	E.	F.	G.	H.
	Total.	Completed Treatment.	Initially Free from Symptoms, Primary and Regional.	Symptom-Free Locally. Distant Metastases.	Recurrence, Primary or Regional Glands.	Symptom-Free. Died of Intercurrent Disease.	Now Symptom-Free, 4 to 8½ Years since Treatment.	Optimal Local Success.
Epipharynx . .	4	2	2	...	...	...	2	2 : 2 = 100%
Mesopharynx .	55	44	25	2	9	3	20	25 : 44 = 56·8%
Hypopharynx .	70	59	31	8	4	10	12	30 : 59 = 50·8%
Intrinsic larynx .	15	11	7	...	...	1	6	7 : 11 = 62·6%
Total . .	144	116	65	10	13	14	40	64 : 116 = 55·1%

at the time of writing, living and free from symptoms—that is, at least nine months after treatment in addition, are those cases dying of distant metastases (10 cases) or of intercurrent disease (14 cases) by *proved* freedom from local disease during six months—that is the sum of columns D, F and G. The ratio of this figure to the number of cases in which treatment is concluded gives the optimal local success, and appears in column H.

The most important weapons in the treatment of cancer at present available, surgery and radiation-therapy, have one important feature in common. They act locally. Their measure of success is their effect in permanently clearing *the treated area* of cancer cells, without reference to the development of distant metastases. The criterion of successful treatment is

the freedom of the patient, until his death from some other cause, from a recurrence in the region treated—"local success." This figure must not be compared with the "lokale Leistungsziffer" of Forssell and Holthusen, which refers only to the primary tumour. It is inadequate where the regional metastases are simultaneously treated, as in almost all cases treated with X-rays. It finds its only proper use in such cases as the radium treatment (or surgical excision) of a carcinoma of the lip when, on occasion, no effort is made to treat the regional gland area.

These figures for optimal local success are therefore given in all the Tables and they provide a useful basis for comparison of various results. It must, however, strongly be emphasised that the absolute position is not sufficiently indicated by this *ratio* in that the number of cases dying of distant metastases or of intercurrent disease accounts for a certain number. For comparison, in the following Table (IV.) the absolute and optimal success after at least nine months' observation are shown. The absolute success is of course the ratio between the number of patients now actually free from symptoms living and the total number of patients referred for treatment. The relative success is—since in all cases at least an effort was made to carry out the treatment—equal to the absolute success and is not given separately.

TABLE IV.

	Per cent. of all Cases. (Absolute)	Per cent. of Cases Concluded Treatment. (Optimal)
Living free from symptoms at least 9 months . .	40 : 144 = 28%	40 : 116 = 35%
No recurrence local or regional at least 9 months (Local success)	64 : 144 = 45%	64 : 116 = 55%

Further, during the year 1931 many more patients were treated than in the previous years and are therefore still in considerable danger of recurrence.

It will be noticed that the use of the word "healing" or "cure" has been studiously avoided. On the basis of a small amount of material, the oldest case of which lies but three years back, this is essential. In the next table are shown the

ultimate results that Coutard obtained. Our provisional results are not quite so good, a fact that is explained firstly in that we had to learn the method, and secondly that we, unlike Coutard, have not the right to select our cases, as a consequence of which our cases are often more advanced in the first instance.

TABLE V.

Épithéliomas de la région amygdalienne, de l'hypopharynx, du larynx, traités de 1920 *à* 1926.

Résultats la Roentgenthérapie après des durées d'observation de guérison variant de 2 à 9 ans.

	2 ans (malades traités de 1920 à 1926).	3 ans (malades traités de 1920 à 1926).	4 ans (malades traités de 1920 à 1926).	5 ans (malades traités de 1920 à 1925).	6 ans (malades traités de 1920 à 1924).	7 ans (malades traités de 1920 à 1923).	8 ans (malades traités de 1920 à 1922).	9 ans (malades traités de 1920 à 1921).
Région amygdalienne .	12 sur 46 (26%)	12 sur 46 (26%)	12 sur 46 (26%)	6 sur 33 (18%)	5 sur 20 (25%)	3 sur 13 (23%)	3 sur 10 (30%)	2 sur 7 (28%)
Hypopharynx . . .	18 sur 89 (20%)	13 sur 89 (14%)	12 sur 89 (13%)	7 sur 69 (10%)	4 sur 45 (9%)	2 sur 26 (7%)	1 sur 18 (5%)	0 sur 7
Larynx	25 sur 77 (32%)	25 sur 77 (32%)	22 sur 77 (28%)	13 sur 60 (21%)	7 sur 43 (16%)	6 sur 31 (19%)	4 sur 19 (21%)	4 sur 8 (50%)
Total des 3 localisations .	55 sur 212 (26%)	50 sur 212 (23%)	46 sur 212 (21%)	26 sur 162 (16%)	16 sur 108 (14%)	11 sur 70 (16%)	8 sur 47 (17%)	6 sur 22 (27%)

(Coutard, 1929).

In order to demonstrate the nature of the material that follows, I have employed the terms "operable," "prognostically inoperable" and "technically inoperable," following in this respect the custom of the institute. They refer to the size and fixation of the growth in every case, and not to its histological nature or to the general condition of the patient. Subjective as it is, this classification conveys a picture of the extent of the growth and yet enables enough cases to be considered together to permit of certain deductions and comparisons. A purely objective classification results in an enormous number of classes with but one or two cases in each. The customary criteria of operability have been considered both in the case of the primary tumour and of its metastases. The case as a whole is placed in the prognostically inoperable group when either the primary tumour or the metastases is prognostically inoperable. When both are prognostically inoperable, the case as a whole appears in the third group.

***A.* Epipharynx.**—The number of cases (4) reported is too small to allow of conclusions. Of great importance is the fact that of the 4 cases 3 were lymphoepithelial carcinomata and the last a lymphosarcoma; that is, all the cases were extremely radiation-sensitive. This is not mere chance, as may be seen in the summary of the material, 1919 to 1928, in the Zürich Clinics (Zuppinger). In 32 cases the histological diagnosis was carcinoma fifteen times and sarcoma fifteen times, with 2 doubtful cases. In 19 cases the preparation could be controlled. *Of these* 19, *no less than* 14 *were tumours of the lymphoepithelial series, the remaining* 5 *lymphosarcomata.* Such tumours metastasise quickly and extensively. Both from this point of view and from the purely technical standpoint, the tumours are not amenable to surgical treatment. In both the cases reported above in which treatment was concluded an extensive tumour, neither operable nor adapted to local radium therapy, was found and, in addition, both showed metastases. That both show a local success must be regarded as good luck.

***B.* Mesopharynx.**—In 44 (80 per cent.) of the 55 cases seen, treatment could be carried to a conclusion. To show the influence of the extent of the growth upon the results, the cases have been grouped according to the principles outlined above. The results of treatment from 1919 to 1928 (Zuppinger) before the introduction of the present method have been similarly grouped and the figures given for comparison. In each case the number of patients treated, the number of local successes obtained and, where suitable, the percentage of local successes are given.

TABLE VI.

Local Success in Cancer of the Mesopharynx.

Series. Stage:	Operable.	Prognostically Inoperable.	Technically Inoperable.	All Cases.
Protracted - fractional Radiation, 1929-31	4 out of 5 80%	6 out of 8 75%	15 out of 31 48%	25 out of 44 56·8%
1919-1928 total. .	4 out of 28	1 out of 25	0 out of 52	5 out of 105 4·8%
Surgically treated .	1 out of 7	0 out of 2	0 out of 0	1 out of 9
Radiotherapy . .	3 out of 21	1 out of 2	0 out of 52	4 out of 96

In the radiotherapy of tumours of the mesopharnyx extensive metastases are a much more unfavourable sign than an extensive primary growth, as is to be seen from the following table, in

which the primary growth and the metastases are separately and independently grouped.

TABLE VII.

Malignant Disease of the Mesopharynx.

1929-1931.	Operable.	Prognostically Inoperable.	Technically Inoperable.
Primary tumour alone .	4 out of 10 40%	8 out of 13 61%	13 out of 21 62%
Metastases alone . .	16 out of 21 76%	6 out of 10 60%	3 out of 13 23%

That the success appears to increase with the severity of the primary lesion must be regarded as a coincidence in that the severe primary growths have displayed more limited metastases, which the above table shows to be of paramount importance in the prognosis.

From these tables it is to be seen that of 160 mesopharyngeal tumours in Zürich during the years of 1918 to 1931, only 33 could be considered as operable, of 28 operable cases from 1919 to 1928 only 7 were in fact operated upon, and of these only one showed a "local success." The figures of other observers, *e.g.* Broder, are of the same order.

Radiation therapy is the treatment of choice for mesopharyngeal tumours.

Malignant disease of the tonsil is the commonest of the mesopharyngeal area and provides in addition a clear demonstration of the importance of tumour histology for the radiotherapist. Further, no consideration of mesopharyngeal malignant disease could be complete without reference to the monograph of Berven on this subject (*Acta radiol.*, Suppl. XI.). A detailed examination of tumours with this localisation is therefore justified. For this purpose our cases will be arranged according to the classification of Berven, and are placed with his for comparison. The comparison is, however, vitiated in that most of Berven's cases have been observed for periods of four years or more since conclusion of treatment, and, therefore, such cases as are now free from symptoms are in all probability permanently healed. The period of observation of our cases varies from nine months to three and a half years, the majority being under two years.

TABLE VIII.

Malignant Growths of the Tonsil.

	Zürich—Schinz. Local Success in :	Stockholm—Berven. Local Success in :
Carcinoma.		
Group I.— No Metastases	1 out of 2	3 out of 6
Group II.— Small mobile localised metastases .	2 „ 4	1 „ 2
Group III.— "Inoperable" metastases, bilateral.	1 „ 6	0 „ 7
	4 out of 12	4 out of 15
Lymphoepithelial and Transitional Celled Carcinoma.		
Group II.	0 out of 1	6 out of 6
Group III.	2 „ 2	0 „ 0
	2 out of 3	6 out of 6
Sarcoma.		
Group I	2 out of 2	8 out of 10
Group II	2 „ 2	10 „ 12
Group III	0 „ 0	5 „ 14
	4 out of 4	23 out of 36

At the Radiumhemmet, Stockholm, as in Zürich, the sensitive growths are treated chiefly, if not exclusively, with deep X-rays. Under the heading carcinoma are included only those results obtained by Berven since the introduction of the 3 gramme radium "bomb" (Teleradium). The use of this source of short-wave radiation, designated by Berven as a step forward in the treatment of carcinoma of the tonsil, and employed from 1924 to 1927, was then given up on account of the shortage of radium, to be re-adopted in 1930. The comparison between the results from Zürich and Stockholm suggests that the protracted-fractional deep X-ray treatment of such tumours is worthy of equal consideration with teleradium.

The results obtained by Berven in 1930 with the new radium bomb (8 cases, 3 without metastases) are very much better; primary freedom from symptoms in 7 cases, all of which at

the time of reporting were still (at least 9 months) free from recurrence.

C. **Hypopharynx.**—During the years 1929-1931 70 cases of malignant disease localised to the hypopharynx were seen. In 59 of these cases (84 per cent.) treatment could be carried to a conclusion, with a local success in 30 (50 per cent.). In Table IX. the results are shown in the separate groups, together with the figures referring to 1919-1928.

TABLE IX.

Malignant Disease of the Hypopharynx.

Series. Stage:	Operable.	Prognostically Inoperable.	Technically Inoperable.	Total.
1929-1931 Protracted-fractional	3 out of 3	11 out of 17 65%	16 out of 39 41%	30 out of 59 50·8%
1919-1929 All cases .	0 out of 17	0 out of 34	0 out of 69	0 out of 120
1919-1929 Surgery .	0 out of 6	0 out of 0	0 out of 0	0 out of 6
1919-1929 Radiotherapy	0 out of 11	0 out of 34	0 out of 69	0 out of 114

It should be mentioned that, of the 1919-1929 material three patients with an operable growth declined the operation. In about twice the number treatment was either impossible from the beginning or was of necessity abandoned in the middle. The results are in no way improved and the protracted-fractional radiation must be regarded as an important advance in the treatment of these growths. The hypopharynx is perhaps the most unsatisfactory situation for new growths. The symptoms are usually very slight until the extension of the disease hinders the vital functions of breathing and swallowing. As a result the greater number of our patients were admitted in a serious condition and presented great difficulties in management. Further, they metastasise rapidly and extensively, and bilateral metastases are common. The figures obtained in the second and third groups are therefore satisfactory on the whole. It should be noted, however, that those cases accessible to radical treatment only by means of total laryngectomy and pharynx resection are counted among the "prognostically inoperable." This operation, a perfect example of cancer surgery, leads to an operative mortality, in the hands of the originators, of 22 per cent. In any case the patient must undergo a series of operations and is severely

mutilated. The success reaches but 10 per cent. in the operated cases and it is doubtful if such an operation is advisable. On the other hand certain cases, by reason of their very limited extent, lend themselves to local excision, an operation practised with excellent success by Trotter, who has recently reported 8 cases with a subsequent freedom from symptoms. He does not, however, state what percentage of cases are amenable to such treatment and in our series they are so rare as to be non-existent. Of the total material, perhaps three fell within this class. Cases in which such procedure is possible are few in proportion to those in which the growth is so extensive as to exclude any such operation. Further, the results of irradiation of such small tumours is probably at least as satisfactory as surgery, especially if comparisons are made with series other than those of Trotter.

Radiation therapy is the treatment of choice in malignant disease of the hypopharynx.

***D.* The Larynx (intrinsic).** — The results of surgical treatment of malignant disease of the larynx are probably not to be equalled by those obtained in any other region of the body. Symptoms are early, extension is slow, and metastases are late—a large number of patients are operable when first seen. On the other hand, the operation is refused by many or the general condition forbids it. Further, in many cases the operation must of necessity be severely mutilating. The condition and results of treatment of this class of patients (11) treated by protracted-fractional X-rays during the period 1929-1931 are shown in the next Table (X.). During this period it was considered advisable to perform a radical operation only two times. Fifteen cases were referred to the radiotherapy institute. In 11 of these treatment could be completed, with local success in 6 cases.

TABLE X.

Malignant Growths of the Larynx (Intrinsic).

Stage.	Operable.	Prognostically Inoperable.	Technically Inoperable.	Total.
1929-1931 Protracted-fractional	5 out of 9 55%	1 out of 1	0 out of 1	6 out of 11 54%

Twenty-two cases were seen between 1919-1928. From the point of view of the tumour and of the metastases all were

operable, though in some cases the laryngectomy and pharynx resection was the operation indicated. Two patients refused all treatment, in five the general condition was too bad to permit of other than expectant treatment, without success. Fifteen cases came for review. Only 8 cases could be submitted to operation, with local success in 4 cases. Of the remaining 7, 4 refused operation and in the remaining 3 the general condition contra-indicated a radical operation. These patients were treated by radiation therapy, with local success in one case. Thus the results obtained between 1919-1928 show a considerable inferiority to those obtained since the introduction of protracted-fractional radiation.

On the other hand, much higher operation rates and local success percentages are published from other clinics. Among the most recent, conspicuous for his advocacy of the more conservative operation, Colledge has reported a series of 60 cases, of which 55 could be submitted to operation, with a local success in no less than 31 (55 per cent.). These results are shown in Table XI.

TABLE XI.

Intrinsic Carcinoma of Larynx (Colledge).

Operation.	Local Success.
Fissure and extended fissure	8 out of 11
Hemilaryngectomy . .	2 out of 3
Total Laryngectomy . .	21 out of 42

Only 2 of the cases operated upon presented metastases, one of these was successful. His operative mortality was only 19 per cent. If these cases are excluded the local success rises to 31 cases out of 45, or 68 per cent., an exceptionally satisfactory figure. These results from Colledge are good indeed, better in fact than those obtained by most other surgeons in this field, and especially good in view of the fact that Colledge limits himself to the least extensive operation that has a chance of success. They lead to the conclusion that all cases without metastases that can be satisfactorily eradicated by means of laryngo-fissure should, in the absence of contra-indications, be submitted to the knife. Nevertheless, by analogy with tumours in other situations, the results of radiation therapy of small growths would probably be almost as good as those from

operation. The more extensive operations are excessively mutilating and do not fulfil the ideal of "restitutio ad integrum."

In doubtful cases, the histological nature of the tumour will be of moment and perhaps of importance in deciding the choice of treatment.

All cases unsuitable for operation on account of their general condition, or those refusing surgical aid, should be radiated. Finally, mention should be made that Hautant has succeeded in performing the radical operation in certain cases in which the size of the tumour has previously been reduced by a full course of protracted-fractional irradiation. Whether the operation is possible, whether it is more difficult or more dangerous, the extent of our material does not permit us to draw a definite conclusion. It is probably somewhat more difficult.

Protracted-fractional X-ray treatment demands consideration in all cases of laryngeal carcinoma and in many it is the treatment of choice.

Conclusion.

Malignant disease of the pharynx and larynx has presented difficulties that have caused an unceasing flow of ideas on its proper treatment. The introduction of radiotherapy afforded a possibility of treatment for those cases regarded as surgically hopeless. Out of the welter of radiotherapeutic methods arose certain well-defined principles leading to a measure of success which in certain areas displaced surgery as the method of choice in the treatment of carcinoma. It is suggested that this position has now been reached in the treatment of malignant disease of the pharynx. With regard to the larynx, surgery remains the best weapon, when it can be employed without grossly mutilating the patient. The limitations of radical surgery and of radiotherapy in this region cannot yet be defined with precision. The great importance of the histology of a malignant growth and a knowledge of its radiobiology has been shown: in many cases this will be a deciding factor in the treatment of laryngeal carcinoma.

The varieties of radiotherapy are without number: we have experience of only one, the protracted-fractional X-ray treatment. The results of the use of radium in malignant disease of the pharynx and larynx during the years 1919-1928 were not encouraging. More recently radium surgery of malignant disease of the larynx has yielded better results, particularly in

conjunction with protracted-fractional treatment of the regional glands.

A series of such cases was presented by Hegener and Holthusen at the Otorhinolaryngological Congress at Bad Ems last May. In 19 cases of carcinoma of the larynx, local success was obtained in 14 (73 per cent.). In this report local radium application after excision of part of the thyroid cartilage is held to be the treatment of choice. The method employed corresponds in principle to those of the forerunners Ledoux, Finzi and Harmer, Seiffert and Halberstädter and others. Nevertheless, examination of the cases reported shows the following treatment methods to which the local success is added in each case (Table XII.).

TABLE XII.

Carcinoma of the Larynx (Hegener and Holthusen).

Treatment.	Success.
1. Radium locally, with surgery of access .	4 out of 5 (80%)
2. Protracted-fractional X-rays, alone .	5 out of 8 (62%)
3. Radium locally, combined with protracted-fractional X-rays	3 out of 4 (75%)
4. Protracted-fractional X-rays after non-radical operation	1 out of 2 (50%)

The indication for the employment of protracted-fractional deep X-rays was a more advanced stage of the disease, particularly the presence of metastases. That is, the less favourable cases. The results of radium therapy alone are indeed good, but the above table serves to demonstrate the number of cases in which homogeneous radiation from an external source is an important factor in the control of the carcinoma. Also at the same Congress various speakers reflected on the possibilities of a laryngeal necrosis following local radium application. Holthusen himself observed one case with a fatal issue, occurring nineteen months after combined radium and X-ray treatment. Local treatment with radium continues to be indicated in small tumours in which accurate application is possible and a homogeneous radiation possible without the employment of such doses as are likely to inflict permanent damage on normal tissue. This class of case is quite rare in the Zürich material (perhaps owing to the constitutional aversion of the Swiss to hospital treatment—the

material referred to consists entirely of hospital patients). In the smaller number of cases in which there is a choice of the radiotherapeutic method the course adopted will depend to a considerable extent on the individual peculiarities of the patient and on the preferences and experiences of the surgeon.

Our experiences encourage further trial of protracted-fractional radiation, the results of which are demonstrated above and bear comparison with other modifications of radiotherapy and with surgery. Except in the particular case of tonsillar cancer, a detailed comparison with other methods of radiotherapy has not been attempted.

The analysis of these results of protracted-fractional therapy is, on the other hand, imperfect in that up to the present no case of a five-year cure can be reported from the Zürich institute. The oldest case was treated but three and a half years ago. Instead of this the figure for "local success" has been considered and an attempt been made to justify it. In any case a local success with the avoidance of a mutilating operation encourages us to persevere with the method. The results of Coutard himself show that the permanent cures bear a by no means unsatisfactory ratio to the local successes. Basing our opinion on the above considerations we would submit that, in almost every case of malignant disease of the pharynx, *radiotherapy is the treatment of choice.* In cancer of the larynx the indication for surgery should be very narrowly drawn.

The results of protracted-fractional X-ray therapy in the treatment of cancer of the larynx and pharynx are not inferior and are often superior to those obtained by any other treatment.

Summary.

1. The principles involved in the *protracted-fractional* method of deep X-ray treatment have been discussed.

2. The details of the method in its application to tumours of the larynx and pharynx, together with illustrative examples showing variation from case to case, are given.

3. An attempt has been made to show the importance of the histological appearances in relation to the sensitivity of the tumour. A classification and illustrations are to be found.

4. The results of the treatment since its introduction to Zürich by Prof. Schinz in 1929 are given and summarised in Table III. (p. 740). 144 cases are reviewed.

5. The local success figure is defined as the number of patients who have become free from signs and symptoms as a result of the treatment and up to the present time have not developed a local or regional recurrence. The optimal percentage local success is the ratio of this figure to the number of cases that have completed the treatment.

6. Since results over a period of five years (absolute healing) are not available, the figures for the optimal local success have been evaluated and its advantages and disadvantages discussed. The percentage local success in this series is 55 per cent.

7. The results are further analysed on a basis of the situation, nature, and extent of the various growths.

8. The results obtained in Zürich, 1919-1928, together with the results of some other authors, are similarly analysed for the purposes of comparison. No attempt has been made to be all-inclusive.

9. The conclusion is reached that the protracted-fractional method of X-ray treatment is the treatment of choice in tumours of the epi-, meso- and hypopharynx. In the case of the larynx it should always be taken into consideration.

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For the complete literature of tumours of the larynx and pharynx up to the end of 1930 the reader is referred to the monograph *Maligne Pharynx- und Larynxtumoren* by A. Zuppinger, published by Georg Thieme, Leipzig, 1913.

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Verfasser stellt die hauptsächlichsten Schlussfolgerungen, die aus seiner Arbeit gezogen werden können, in folgender Weise zusammen:—

1. Die Grundsätze der protrahiert-fraktionierten Methode der Röntgentiefenbestrahlung wurden besprochen.

2. Die Einzelheiten der Anwendung dieser Methode bei Tumoren des Larynx und Pharynx werden bekannt gegeben. Ebenso werden Beispiele mit ihren Abweichungen von Fall zu Fall mitgeteilt.

3. Es wurde versucht die Wichtigkeit des histologischen Bildes in Bezug auf die Strahlenempfindlichkeit der Geschwülste darzulegen. Eine Einteilung sowie Abbildung werden beigefügt.

4. Die Ergebnisse der Behandlung seit ihrer Einführung durch Prof. Schinz in Zürich im Jahre 1921 werden mitgeteilt und zusammenfassend in Tafel III. wiedergegeben. Es wird über 144 Fälle referiert.

5. Unter der Ziffer der "Lokalerfolge" sind die Zahlen derjenigen Patienten zu verstehen, die als Folge der Behandlung symptomlos wurden und bis jetzt kein lokales oder regionäres Rezidiv aufweisen. Der Prozentsatz der Lokalerfolge ist das Verhältnis zwischen der lokalen Erfolgsziffer und der Zahl der Kranken, welche die Behandlung zu Ende geführt haben.

6. Da die Ergebnisse über einen Zeitraum von 5 Jahren (vollständige Heilung) noch nicht erhältlich sind, wurden die Zahlen der lokalen Erfolge berücksichtigt und auf ihre Vor- und Nachteile untersucht. Der Prozentsatz lokaler Erfolge beträgt in dieser Serie 55%.

7. Die Ergebnisse werden in Bezug auf die Lage, Natur und Ausdehnung der verschiedenen Geschwülste untersucht.

8. Die in Zürich in den Jahren 1918-28 erhaltenen Resultate werden mit denjenigen einiger andern Autoren zusammengestellt, besprochen und untereinander verglichen. Es wird kein Anspruch auf Vollständigkeit erhoben.

9. Es wird die Schlussfolgerung aufgestellt, dass die protrahiert-fraktionierte Methode der Röntgenbestrahlung bei Geschwülsten des Epi-, Meso- und Hypopharynx die Methode der Wahl darstellt. Bei Larynxtumoren sollte sie ebenfalls in Betracht gezogen werden.

L'auteur cite les conclusions principales à déduire de son exposé ainsi qu'il suit:—

1. Les principes à propos de la radiothérapie profonde par une méthode fractionnaire prolongée ont été discutés.
2. Les détails sont exposés des méthodes d'application aux tumeurs du larynx et du pharynx démontrant les variations entre les différents cas.
3. On a essayé de démontrer l'importance que jouent les apparences histologiques par rapport à la sensibilité de la tumeur. On y trouve également une classification et des figures.
4. On trouve du tableau 3 un résumé des résultats du traitement depuis que le professeur Schinz en 1921 l'avait présenté à Zürich. On passe en revue 144 cas.
5. Les cas réussis localement sont determinés par le nombre de cas qui se sont trouvés débarrassés de signes et de symptômes comme résultat du traitement, et qui jusqu'à ce jour n'ont pas eu de récidive soit local soit régional. Le pourcentage des cas réussis localement est le rapport de ce chiffre au nombre de ces cas dont le traitement a été conclu.
6. Comme on n'a pas encore atteint les 5 ans de guérison définitive, les chiffres du succès local ont été notés et on en discute les avantages et les désavantages du traitement. Le pourcentage des cas localement guéris dans cette série est de 55 %.
7. On analyse aussi les résultats obtenus selon la situation, la nature et l'étendue des tumeurs différentes.
8. Les résultats obtenus à Zürich 1919-1928 ainsi que ceux obtenus par quelques autres auteurs sont analysés de la même façon pour servir à titre de comparaison. L'auteur ne cherche pas à faire règle général pour tous les cas.
9. On arrive à la conclusion que la radiothérapie par la méthode fractionnaire prolongée est la méthode de choix pour les régions de l'épi- du meso- et de l'hypo-pharynx. Quand il s'agit du larynx, il faut toujours y penser.