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ON THE USE OF RADIUM TO EFFECT AN ATROPHY OF PHARYNGEAL LYMPHOID TISSUES— A TOPICAL REVIEW.

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It is to be regretted that more of the competent laryngologists have not undertaken the investigation of the use of radium to effect an atrophy of tonsillar and adenoid tissue.

In order to keep the chief points in mind, it will be profitable to briefly review the embryology, anatomy, physiology and pathology of the tonsil.

Embryology and Anatomy—The development of the tonsillar ring begins in foetal life. Encircling the opening of the pharynx, lying in the mucous membrane is a ring of lymph follicles, sometimes called the ring of Waldeyer. Certain parts of the ring become well defined, lymphoid structures, of which four are of importance:

1. The tonsil at the apex of the ring in the pharyngeal vault.
- 2 and 3. The two lateral masses of tonsillar tissue between the pillars of the fauces.
4. The single lingual tonsil at the base of the tongue.

Other parts of the ring are represented in scattered islands of lymphoid tissue about the Eustachian tubes, in the fossae of Rosenmuller and along the lateral folds of the pharynx. During the second decade of life, the upper part of the ring tends to retrogress and the lower portions remain, though becoming gradually smaller as a rule.

The crypts of the tonsils are developed from invaginations of the epithelium and vary in size from almost microscopical ducts to the large subdivided pockets of the faucial tonsil. Around these crypts lymphoid tissue is built up, and between them interstitial connective tissue extends to the supporting mucous membrane.

Physiology—The physiology of the tonsillar ring has long been a mystery. Its position in the portals of the mouth and nose, its constant presence, its periods of growth and involution suggest that it may have a definite function, acting complementary to, or in the same manner as lymphoid tissue in other parts of the body. The physiological function usually ascribed to it, is that of protecting

Figure 1. To show the relative size and position of the pharyngeal tonsil in the vault of the pharynx.

the body against infection, especially in childhood. It is possible that pathogenic bacteria caught in its crypts may stimulate the body's immunizing agents against systemic infection by like organisms. Yet the removal of large amounts of this tonsillar tissue has not been shown to produce any decided ill effects, on the contrary it is taken away to the advantage of the patient in practically all of its diseased conditions. *No operation can remove all of the lymphoid tissue in the pharyngeal mucous membrane, and when the excision of large amounts is done in early life, the outlying parts of the ring appear to be stimulated to growth and hyperplasia.*

THE TONSILLAR RING.

TAKEN FROM COOLIDGE.—DISEASES OF THE NOSE AND THROAT.

Figures 2 and 3. Diagrams illustrating the development of the tonsil (Barnes). The left-hand figure in each row represents the sinus tonsillar at the fourth month of foetal life before the appearance of tonsillar tissue. The succeeding figures show the gradual development of the tonsil and explain the relationship which it assumes to the surrounding tissues. The upper four figures are in cross section and show the development of the tonsil and plica. The lower row, in longitudinal section, shows the development of the tonsil and the formation of the supra-tonsillar fossa. A, Sinus tonsillar; B, Fauces epithelium; C, Fibrous mucosa; D, Muscle fibers of anterior pillar; E, Posterior pillar; F, Plica triangularis; G, Superior constrictor of the pharynx; H, Epithelial bud—the anlage of the crypt; I, Fibrous trabecula springing from M—the capsula; N, Anterior fossa; P, Posterior fossa; S, Muscle fibers; T, Supra-tonsillar fossa.

The great majority of children have more adenoid tissue in the vault and faucial tonsils than is generally supposed. The pharyngeal tonsil is present and of considerable size up to the age of nine to twelve. After the age of 25 to 30 it should not be visible. The faucial tonsils, in childhood, weigh from two to three grams each, and persist much longer than the pharyngeal tonsil. The lingual tonsil develops last of all and is quite variable in size.

Histology—Lymphoid tissue constitutes the bulk of the tonsil, covered by soft, moist, entodermal epithelium, resting on a connective or reticular tissue layer. The *tunica propria*. A structureless basement membrane is often present immediately beneath the epithelium. The epithelium, basement membrane and tunica propria, constitute the mucous membrane, and in dissection, would be stripped off as a single structure. Beneath the mucous membrane and attaching it to the underlying, deep structures is a very vascular connective tissue, which forms the capsule of the organ and through which it sends trabeculations to mucous membrane.

The epithelium of the tonsils is a stratified epithelium of many layers, with flattened cells on its smooth free surface, and columnar cells beneath. This epithelium lines from ten to twenty *tonsillar pits* or *fossulae* (crypts). These are irregularly tubular and often branched. Many lymphocytes penetrate between the epithelial cells and escape from the free surface into the saliva becoming "salivary corpuscles." In places, the tonsillar epithelium is so full of lymphocytes as to appear disintegrated. In the reticular layer of the tunica propria, especially about the crypts, there are many lymph nodules, some of which are well defined, with germinative centers, but many others are fused into indefinite masses. This lymphoid tissue constitutes the bulk of the tonsil.¹

The structure of the lingual and pharyngeal tonsils is much like that of the palatine or faucial tonsils.

Pathology—In certain cases such as acute tonsillitis, hyperkeratosis, (parakeratosis) and often in simple hypertrophy, the faucial tonsils participate in the general disturbance of the whole ring. In more indefinite infections, the relatively poor drainage of the crypts and the large mass of the faucial tonsils make them more often the seat of pathological processes than is the case with the rest of the ring.

Diseases of the tonsils may be grouped into acute and chronic, the former including acute tonsillitis, peritonsillar abscess, and those cases of acute local infection, such as diphtheria, Vincent's angina,

etc. The chronic diseases include hypertrophy, keratosis (or parakeratosis) and cases of periodic hyperplasia or septic absorption. If the tonsil allows infection to pass through it into the sys-

Figure 4. "Diagram of a section of a faucial tonsil, showing crypts, follicles and capsule. This tonsil is of the submerged type and the crypts irregular and dilated." (Coolidge.)

Figure 5. Large prominent tonsils.

tem or, if mechanically, it is obstructive, it must be looked upon as pathological. Syphilis, tuberculosis, sarcoma and carcinoma are rather uncommon pathological processes of the tonsil.

Coolidge² states as follows:

1. "Tonsils should be removed if serious symptoms can be logically attributed to them. The more serious the symptoms and the more direct the connection, the more imperative is the operation.
2. "They should be removed for recurring peritonsillar abscess.
3. "They should be removed for recurring and persistent cervical adenitis that cannot be accounted for by a focus in the teeth, vestibule, scalp, nose, naso-pharynx or ears.
4. "They should be removed for recurring sub-acute tonsillitis.
5. "They should be removed if it is believed or even seriously suspected that they are the entering point of constitutional infec-

Figure 6. Tonsils of the same size as in the preceding figure, but submerged or buried in the palate.

tion. It is perhaps better to sacrifice many innocent tonsils rather than to allow one guilty one to escape, but it is also true that every unnecessary operation does a little harm to medical science. It is unfortunate that we can never be sure, by its appearance that a tonsil is innocent, and not very often that it is guilty.

6. "Very large tonsils should be removed, as experience proves that persons are better off without them.

7. "Tonsils which are wholly exposed may be obstructive and require removal in that account irrespective of size. It is generally the deeper portion that is the more important to remove.

"Tonsillectomy should be looked upon as a serious operation. As in the majority of cases, patients undergo the operation with little disturbance, and the results are apparently all to the good. The removal of the tonsils is not infrequently advised with the feeling that the operation is insignificant, and that the tonsils are in themselves a disease. Complications may occur in tonsillectomy, and the convalescence may be very slow."

Regardless of its future as a therapeutic agent, one of the permanent contributions of radium therapy has been the demonstration of certain biological properties of tissues which were previously unrecognized. It was observed that certain tissues were *resistant* to even large doses of radiation, while others were quite *susceptible* and underwent resolution or retrogression with remarkably small units of beta, gamma or X-rays.

In general, the structural characters, which determine susceptibility to radiation are a cellular nature; undifferentiated form of cells; hyperchromatic nuclei; rapid growth with abundance of mitoses; vascularity, especially when due to an abundance of delicate capillaries; and absence of much inter-cellular substance. (Ewing⁴). It was the presence of this histological picture, wholly or in part, in malignancies which responded quickly to radium that lead certain authors to assert that radium was selective in its action for certain types of cells.

Satenstein and Remer⁴ state that, "Acute and subacute inflammatory tissues are characterized by lymphocytes—round cells. They are the least resistant of all pathologic cells and are the most readily influenced by therapeutic measures."

On the other hand, tissues prove relatively insusceptible when the cells are differentiated, adult in type and contain small amounts of chromatin in the nucleus; when they grow slowly, and mitoses are few; when the blood supply is through well formed adult vessels; and when there is much intercellular substance. (Ewing³).

How do X-rays and gamma rays act on living tissues? Regaud⁵ states that the little penetrating, and therefore readily absorbed, rays have a general caustic action, but the more penetrating rays have an "elective cyto-caustic action." There is a long range of radio-sensibility for animal cells, ranging between the most radio-sensitive (such as certain sex and leucocytic cells), and the least radio-sensitive (such as muscle fibers and nerve cells). The radio-sensibility, too, is a property of the nucleus, and is inherent in certain states or temporary physiological periods of cell life, the most

important and best known of which is the state of reproduction. Arguing from these premises, Regaud⁵ asserts that X and gamma rays of very short wave length are elective poisons for nuclear chromatin. Hence, the rays suppress or suspend reproduction in lymphoid tissue, which is likewise shown to be highly radio-sensitive. Adult connective tissue and epithelial cells stand much lower in the scale of radio-sensibility (more resistant) than leucocytic elements and young endothelial cells and fibroblasts.

It should, therefore, be possible to produce a marked retrogression of lymphoid and leucocytic elements in tonsillar tissue without causing a solution of continuity of the connective tissue elements.

Murphy, Witherbee, Craig, Hussey and Sturm of the Rockefeller Institute⁶ made a joint study of a series of forty-six cases of diseased tonsils, treated with fairly well filtered X-rays, and proved that they could:

1. Bring about a definite diminution in the size of the hypertrophied tonsils,
2. That with such atrophy there was evidence of less occluded debris in the crypts with,
3. A diminution in the exudate and sepsis, particularly in reference to hemolytic streptococci,
4. Without producing undue reaction either constitutionally or locally.

These authors do not infer that the X-ray producing the lymphoid atrophy has any bactericidal action.

Their method is open to the criticism that the rays must penetrate more than an inch of normal tissue to reach the target, in the case of the faucial tonsils, and two to three inches in raying the adenoids through the back of the neck, with the consequent loss in intensity, and dispersion. The probability of temporary or permanent epilation and cutaneous atrophy of the area of the skin portal is not remote. There is some danger of unfavorable effect on the parotid gland, the lower pole of which is traversed in such treatment.

Paccini⁷ reported, favorably, a method combining the use of ultra violet-rays to the surface of the tonsil supplemented by X-ray following the Murphy-Witherbee⁶ technique; claiming that there was a direct bactericidal effect of the ultra violet-rays in the surface layers of the tonsillar epithelium. A serious doubt is raised in the minds of many, that the depth of penetration of such ultra violet

rays below the surface is not sufficient to cause a sterilization of the crypts. The method is open to the criticism that such treatments must be repeated time and time again.

Many other reports of the use of X-rays in the treatment of tonsillar hypertrophy have appeared, but without adding materially to the data above given.

A brief review of the bactericidal effect of beta radiation is here indicated, in view of the fact that there is prevalent among many physicians the opinion that such rays have little, if any, sterilizing properties.

It is sufficient to quote the very responsible authors, Colwell and Russ⁸ and Chambers and Russ⁹, on this point.

"SHOWING TIME REQUIRED FOR STERILIZING EFFECT PRODUCED BY 0.5 MILLI-CURIE PER CUBIC CENTIMETER."

Organism	Time	
<i>B. coli communis</i>	1 hour	5 min.
<i>Staph. aureus</i>	2 hours	0 "
<i>B. pyocyaneus</i>	3 "	10 "
<i>B. anthracis</i>	3 "	20 "
<i>B. tuberculosis</i>	4 "	0 "

"The number of organisms in the suspension was approximately one million per cubic centimeter."

Quoted from Colwell & Russ, "Radium X-rays and the Living Cell," page 146.

Recently the practical application of this bactericidal action of beta rays has been demonstrated by Marshall¹⁰ in sterilizing apical abscesses by the injection of even such small amounts as .06 to .08 milli-cures of emanation and sealing the canal. Bacteriological examination of the treated canals showed sterility in 85 per cent of the cases.

There is no evidence to show that infection which has been introduced in buried tubes of emanation has persisted. In fact, the necrotic tissue surrounding such buried tubes, (which would make an ideal culture media), has repeatedly been shown to be sterile.

Bagg¹¹ has shown that upon embedding from .5 to 1.0 milli-curie in tiny capillary glass tubes in muscle (radio-resistant tissue), there is produced a zone of necrosis of about 5 millimeters in radius, about such a spicule. The necrotic center is surrounded by a zone of intense leucocytic infiltration, in which is carried on active phagocytosis. The destroyed cells in the center are generally absorbed without infection or surface sloughing.

ABSTRACTS OF ARTICLES DEALING WITH THE USE OF RADIUM IN THE
TREATMENT OF TONSILS.

It is a singular coincidence that the first physician to use radium therapeutically, (Reported by Chase)¹² in this country, (1900) and also, the first to use radium within the mouth to effect an atrophy of hyperplastic tonsillar tissue are the same; Francis H. Williams, M. D., of Boston. The first record of a design for a tonsil applicator, and the use of radium in a series of cases, was made by Doctor Williams¹³ in March, 1921.

The following is an abstract of Doctor Williams¹³ preliminary report in his own words:

Figure 7. To show the Action of Beta Rays on *Staphylococcus Pyogenes Aureus*. (Colwell and Russ.)

"The rays from radium cause a retrogression in the growth of lymphoid tissues, of which the tonsils and adenoids are made up to a large extent, and can be applied directly to the tonsils and adenoids, and neighboring parts being protected by lead, that is to say, the radium container is covered with lead except on the side through which is desired that the rays should issue, allowing the maximum radiation to reach the tonsils and adenoids, and the minimum other parts.

"I have used 50 milligrams of bromide of radium," (radium bromide contains approximately 53 per cent of radium element, so that the amount used here would approximate 26 milligrams of radium element), "in a flat container, with the rays filtered by 0.83 millimeter of aluminum, held directly against or near the tonsil. The radium should be withdrawn every few minutes, or as often as is comfortable for the patient, until the total exposure of 15 minutes,

more or less as required, has been reached. Improvement follows promptly, but the ultimate results may be expected only after some weeks. Guided by more than 17 years' experience in the use of radium, it seems to me better not to attempt complete healing by one treatment, for the present at least, but rather to give two or perhaps three treatments as patients and conditions differ.

"It may prove more convenient to use a container by means of which both tonsils may be treated at the same time. I have devised one to be held midway between the tonsils, which consists, in general, of a disk of lead, (not more than 2 centimeters in diameter and about 1 centimeter thick, more so in the middle), with a hole bored through its center, somewhat flared at each end, for the exit of the rays, and another bored from the outer edge radially

Figure 8. Design of applicator suggested by Doctor Williams for treating both tonsils at the same time. Below 1. is a small bulb at the end of the bent portion of a glass tube, for containing the radium. The straight end is inserted into a metal handle about 30 cm. long, of which only 7.5 cm. are shown, by lifting the spring at 2, and is held in place by a narrow strip of plaster wound around the glass and metal between 2 and 3. The radium is kept in position in the bulb by stuffing the tube with spun glass, and more spun glass is pushed in until the tube is nearly filled, the end being closed with a cork, instead of sealed off as shown in the cut. An aluminum cap, to act as a filter, is slipped over the bulb and then the bulb and bent portion of the tube are enclosed in sheet lead, except the lower end of the bulb. The lead should extend more or less beyond the bulb, according to the size of the area to be treated.

to a little beyond the center. The tube containing the radium may be slipped into this end and the opening afterwards closed by screwing a metal handle part way into it. The uvula, the back of the throat, and parts behind it are thus protected by about 1 centimeter of lead. When treating one tonsil only, the opening towards the other may be closed with a plug of lead. Appropriate filters should be used.

"Before applying the radium the throat should be moistened with a suitable solution of cocain to prevent gagging from the insertion of the container. All instruments should be covered with two thicknesses of rubber, and for this purpose, two rubber finger cots are stretched over them and far down on the handle, where they may be secured by a strip of plaster.

"For the tonsils, radium, if properly used, I consider the safest, and that it will probably prove to be the best treatment for many patients.

"While not coming within the title of this paper, it is noteworthy that after treatment by radium, I have observed striking improvement in acute and sub-acute tonsillitis."

Simpson¹⁴, of Washington, D. C., reported a series of cases treated by means of, "a flat dermatological, 30 milligram, double strength radium applicator (plaque), covered with only a single layer of sterile rubber tissue." "A convenient handle is supplied with the applicator which enables the patient to hold the unscreened radium directly on the tonsils for an hour. With this original technique, it is perfectly remarkable how quickly the tonsil begins to shrink and show other atrophic changes. A mild reaction which

Figure 9. Plaque applicator faced with 1 millimeter of Redmanol containing 30 milligrams of radium element designed by Doctor Simpson¹⁴ to treat hypertrophied tonsils.

turns white, is to be seen where the radium has been held. This slight irritation of the tonsil disappears in two or three days." "Swabbing the throat and tonsil with a two per cent novocain solution will usually eliminate any gagging."

"By using the unscreened radium applicator on the surface of the tonsil, combined with three points Hampson X-ray three millimeters aluminum pastile on the skin, and covered with two layers of chamois skin externally, I get a cross-fire of radium and X-rays which is concentrated and centered on the tonsil itself." Simpson states that he is positive that he can cause the complete atrophy and disappearance of any but a *fibrous tonsil*, in from one to three treatments. In his article, he neglects to mention the exact radium or X-ray technique used, it is inferred, however, that the radium applied is about 60 milligram hours to each tonsil. The accompanying illustration, Figure 9, shows the applicator that was designed by Doctor Simpson for treating the tonsils.

In a personal communication, Mr. C. F. Whittemore, a radium physicist, has submitted the accompanying photograph, Figure 10, of an applicator for utilizing chiefly beta radiation to treat tonsils. I am assured that such an applicator will not screen off more than 50 per cent of the available beta rays, which is about equal to a plaque faced with .4 millimeter of aluminum.

The advantages claimed for such an applicator are, that in it may be placed the glass capsules containing the radium salt or emanation as used in tubular applicators, which permits the passing of about 100 per cent more beta radiation than would be available through .5 millimeter of silver.

Wells¹⁵, of Washington, D. C., also reports a series of cases of hypertrophied tonsils treated with radium. In a personal communication, he states that the technique usually followed is to embed

Figure 10. Applicator plaque for holding two glass capsules of radium to treat tonsils. The only screening interposed between the glass radium containing tubes is 0.1 millimeter of monel metal. The openings in the plaque are closed securely by placing the guard (seen just to the right of the plaque in the illustration), in position and inserting the handle, holding the two parts firmly together.

into each tonsil three 10 milligram needles, from above downward, leaving them in position from one to two hours. In other words, it requires about 60 milligram-hours to produce an atrophy of the average tonsil, when needles are embedded directly into its substance.

In regard to the effect he states as follows:

"For the purpose of comparison, it has been my habit to begin always with the larger of the two tonsils, and the effect is always impressive when at the next sitting we observe that the proportion is reversed and that the previously larger tonsil has now become the smaller one. In addition to mere reduction of size, a decided difference is remarked in the appearance of the organ. A tonsil that previously presented an irregular, nodulated surface, or perhaps

has been of the so-called ragged or spongy type, now appears smooth, firm and pale. Very important proof that the atrophic process has successfully attacked the diseased lymphoid structure, is found in the progressive lessening of colonies of bacteria, and especially the fact that we can no longer obtain pathologic exudate from the crypts on pressure."

Most of the standard needles, containing ten milligrams of radium, are from 25 to 29 millimeters in length and have the radium packed into a space in the barrel, of about 8 to 10 millimeters nearest the point. In order, then, to have that portion of the needle containing the radium in contact with the tissue it is desired to effect, it is necessary to have the point of the needle penetrating 3 to 5 millimeters beyond.

A very complete review of the tonsil by Keiper¹⁰, but without bibliography, passes of irradiation treatment of hypertrophied tonsils, with the statement that, "This certainly ought to be tried out, for it may prove to be a very valuable method."

The particular advantage of radium, in direct contact with tonsillar tissue over X-ray applied from without, lies in the fact that with a given quantity of radium or emanation, the quantity of radiation is not so variable, and use can be made of beta rays which have a direct bactericidal effect and do not have enough penetration to cause any destruction of the neighboring structures.

With this in mind, the writer would like to suggest that men who have emanation available try with him, the use of bare tubes containing 0.2 to 0.3 milli-curies buried in the tonsil, one such spicule for approximately one cubic centimeter of the bulk of the tonsil. In cases of moderate sized tonsils, 0.2 to 0.3 milli-curies embedded in the upper and lower poles of each tonsil is advised.

The introduction of bare tubes of 0.3 millimeter in diameter and 3.0 millimeters in length is easily accomplished by means of the tiny trocar-stylette introducer, herewith illustrated. (Figure 11). It is only necessary to swab the surface of the tonsil with a cotton wound applicator moistened in 1:1000 adrenalin and dipped in cocaine (hydrochloride) crystals. The operation of inserting the bare tubes should not take more than five minutes and the patient is not in the least discomfited.

Such an application makes use of the maximum of beta radiation with the least possible destruction or injury of neighboring tissue.

In the course of time and with sufficient dosage, (repeated if necessary), it is certain that we can obtain an atrophy of the tonsil,

which we may liken to the normal physiological retrogression, and that all local evidences of disease disappear.

We need one further evidence of the value of this method; namely, the disappearance of systemic involvements of varying character, that are known to have had their origin in tonsillar disease. This appears, from limited observation to be true, but more experience is necessary before one may speak of this phase of the subject with a proper feeling of conviction and authority.

Figure 11. Bare tubes of emanation (spicules) forceps and introducer (trocar-stylette), for embedding bare tubes of emanation subcutaneously.

SUMMARY.

1. We have briefly reviewed the Embryology, Anatomy, Physiology and Pathology of the lymphoid tissue of the pharynx.
2. That "it is better to sacrifice many innocent tonsils than to allow one guilty one to escape" surgery, and that the operation is not insignificant or free from complications.
3. That no tonsillectomy can remove all of the objectionable lymphoid tissue in the pharyngeal mucous membrane, and when the excision of large amounts is done early in life, the outlying parts of the ring appear to be stimulated to growth.
4. Regardless of its therapeutic properties, the demonstration of certain biological properties of cells by radium has been a permanent contribution to science.
5. That tonsillar tissue is probably one of the most "radio-sensitive" tissues of the body.

6. That it is possible to produce marked retrogression in leucocytic elements and tonsillar tissue with X-rays and radium.

7. The use of radium in affecting an atrophy of tonsils is not new and that its use is founded on sound biological principles.

8. Suitable means of application have been devised.

9. That the use of radium to treat hypertrophied tonsils is superior to the use of X-rays in that its use entails none of the possible dangers.

10. Radium has the advantage in that its radiation is constant. It may be distributed in plaques, tubes, needles or bare tubes of emanation which may be applied directly where the effect is desired without injury to the surrounding parts; and that, in certain forms of application, use may be made of beta radiation which has a decided bactericidal effect.

With all due allowance for ethical practices and conservatism, the fact remains that our patients are demanding that they be more fully taken into consideration as individuals and not as cases, and that they be subjected to lines of treatment based on natural laws. Blind indeed is the physician, specialist or general practitioner, who has not sensed the unmistakable awakening to a fuller realization of the truths of his science, as at present understood, based on rational knowledge of the basic subjects of our medical studies.

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