

D. Miscellaneous.

CASE IX.—Sergeant C., 1st Royal Munster Fusiliers; second admission for M. T.; temperature 103°. Quinine given at first and discontinued when spleen was found enlarged 2 in. below costal margin; hard on palpation, with well-defined border; painful. Exposure five minutes on two consecutive days. Result: Immediate relief of pain and disappearance of enlargement; temperature dropped to subnormal after second day; no further rise in temperature; convalescent.

CASE X.—Gunner P., 91st Battery R. F. A.; admitted with B. T.; temperature 100°. Complaining of dragging pain in the splenic region; spleen enlarged below costal margin. Exposure three minutes. Immediate relief of pain; disappearance of splenic tumour; temperature dropped to subnormal, no further rise; convalescent.

CASE XI.—Bombardier L., 91st Battery R. F. A.; admitted with B. T.; temperature 100°. Complained of dragging pain in region of spleen; spleen enlarged 1 in. below costal margin. Exposure three minutes; relief of pain; disappearance of splenic tumour; temperature dropped to subnormal, no further rise; convalescent.

REMARKS.

Our experience has been that the application of α rays in cases of malarial fever relieves splenic pain and reduces recent engorgement; that the temperature falls and does not usually rise again; and that recovery is not attended by the anaemia usually present in cases treated with quinine. We have not had to fall back upon quinine in cases treated by the α rays, while we have had cases which resisted quinine and yielded promptly to the rays (quinine being discontinued).

We have 5 cases (natives) of chronic induration of spleen (malarial) under treatment, but the progress made has not been sufficiently marked to enable us to make any definite statement as to the special value of α rays in such cases. But we are so impressed with the results in malarial fever cases that we have prepared this record in the hope that our experiences may be obtained by others, and on a more extended scale.

THYROID EXTRACT IN CARCINOMA.

BY

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RHYL.

ALTHOUGH organo-therapy in some form or another has existed from most ancient times, even amongst savages, the method as at present practised is of recent origin, and of all extracts thyroid gland is still the most successfully used, and for certain conditions, such as myxoedema and certain forms of goitre, a specific, even more so than potassium iodide for syphilis or the salicylates for rheumatism. There are many other conditions in which the gland has been more or less successfully employed, though perhaps without definite specific action—for instance, oedema, psoriasis, uterine fibroid, some forms of retarded development in children, and many other cases associated with defective metabolic processes—which is well illustrated by the following most striking case of multiple carcinoma of the skin and subcutaneous tissue. I am aware that this is only a single instance, but the result was so gratifying that a record of the notes of the case may prove interesting.

The patient, a widow aged 61, gave the following history: In November, 1899, she had a large pimple in the right axilla, and at the same time two nodules below the skin on the left side of the chest in the axillary line. The latter seem to have disappeared after the application of some ointment. The lump under the right axilla, however, continued to grow, until it attained the size of an ordinary marble, of a dark purple colour, and at times this was very painful. At this period the general health remained good, apart from an occasional feeling of extreme cold associated with a greenish pallor of the face. The lump under the right axilla became so large and painful that in June, 1900, she went to see Mr. Robert Jones, of Liverpool, who advised immediate operation. This was done. In October of the same year she again consulted him for a growth under her left breast. She was urged to go again in a fortnight, to have this also removed, but, as in the meantime another growth occurred in the left side of the upper part of the abdomen, the patient was discouraged and did not go. During the months that followed several other fresh growths appeared under the skin, two on the right side of the chest, one on the front of the chest above the breast, two on the left side of the chest, and last of all one under the right armpit. This made eight growths in all, varying in size from a walnut to a Tangerine orange.

By this time her general health was suffering severely. I saw her in June, 1901, and found the growths as above described. The growth in the right axilla was the largest of all, fixed and painful, and was the size of a tennis ball; it prevented the arm from being brought to the side, and had recurred at the site of the scar of the previous operation performed by Mr. Robert Jones (in June, 1900). The other growths were smaller, about the size of filberts and walnuts. They were not painful, but were tender on pressure and hard to the touch, and seemed characteristic of scirrhus cancer.

The larger growth (axillary) was to all appearances not far from ulceration and breaking down. The patient appeared to be very anaemic, having a sallow greenish-yellow colour; her pulse and respiration were quickened, and her temperature varied from about 99° to 101°. Sickness was frequent; the appetite was very poor—she was scarcely able to retain anything. The patient had lost 3 st. in weight.

As she had been operated on twelve months previously, with the unfortunate result mentioned, and owing to the dissemination of the growth and her feeble state of health, it was useless to suggest further operative interference, so I decided to try the effect of thyroid medication. Owing to her enfeebled state of health I administered tabloids of thyroid gland with extreme caution, starting with grains v daily, gradually increasing the dose to grains x, and finally to grains xv daily.

To my surprise the patient quickly showed signs of improvement; the palpitation, sickness, and emaciation gradually disappeared *pari passu* with the gradual disappearance of the growths. At the end of August, 1901, the growths had entirely disappeared, the patient was practically well and had recovered her lost weight of 3 st., and up to the present date is quite well, not having suffered in any way from them since. I was so gratified with this result that I almost doubted the nature of these growths, so I wrote to Mr. Robert Jones of Liverpool, in December, 1903, for his opinion of the growth he had removed in 1900. The following is his answer to my inquiry:

It was unquestionably a carcinoma, although I cannot quite recollect any of the pathological details. It was examined by a couple of men besides myself. Some time later there seemed to be a recurrence of the growth trouble, and I recommended removal of the lump. However, she would not agree to that, and I have often wondered what happened to it. This was some years ago; can you let me know in what spot the growth has recurred? Is it in the neighbourhood of the scar, which you will find in the fold of the axilla, or is it in the breast tissue?

After reviewing the results of thyroid administration obtained by other observers, much less after the result in the case I have just recorded, any impartial observer must conclude that thyroid organo-therapy cannot in any sense supersede the well-recognized methods of surgical procedure in operable carcinoma. The free removal of the growth during the operable stage must stand as the soundest and most hopeful measure of curative treatment. When, however, complete radical treatment is out of the question, and when operative measures are refused by the patient, even in the operable stage, thyroid administration offers some hope of checking the rapidity of the growth, favouring spontaneous cure, and possibly achieving the slow but absolute disappearance of the growth.

There are now on record a number of well-authenticated cases of carcinoma, in addition to my own case, which have to all appearance entirely disappeared under the administration of thyroid extract. Their numbers are not great, but they are sufficiently striking to lead me to conclude that the association of thyroid administration with the cure is more than a mere coincidence.

A still larger number of cases of carcinoma have been recorded where thyroid administration was followed by disappearance of secondary nodules, increase of weight, loss of pain, and other signs of marked local and general improvement, but not complete cure of the growth. In these cases treated by thyroid there appeared to be established a negative phase of growth in the neoplasm, during which the nodules or mass ceased to grow—or retrogressed—and in many cases underwent a spontaneous cure.

Many of the cases which were thus favourably influenced by organo-therapy had double oöphorectomy performed previous to the administration of this animal extract. Double oöphorectomy found its great advocate in Beatson, and was applied particularly to women below the menopause. Beatson, supported by other observers, such as Herman, Siles, Chicken, McAdam Eccles, and

others, advocated oöphorectomy with subsequent thyroid administration as a justifiable procedure to recommend to patients short of the climacteric who were suffering from inoperable carcinoma, particularly of the breast.

It was found by almost all observers that after the menopause there was little or no advantage in performing double oöphorectomy, simply because the ovaries had ceased their active sexual life and ceased to influence the metabolism, and more particularly the proliferating properties of cells of the body.

The case I have just recorded is an example of carcinoma arising after the menopause, and was treated after recurrence of the growth, following operation, by thyroid treatment alone. All the observers—such as Beatson, Herman, and Stanley Boyd—who have employed oöphorectomy combined with thyroid extract are agreed that the results are much better in the combined treatment than where oöphorectomy is employed alone.

In Mr. Stanley Boyd's series of 40 collected cases of cancer of the breast treated by oöphorectomy, or by oöphorectomy and thyroid extract combined, the value of thyroid extract was strikingly exhibited in the 17 cases of this series which were favourably influenced by oöphorectomy (in at least 12 of them this was combined with thyroid administration), whereas in the remaining 23 cases which appeared to derive little benefit from oöphorectomy, thyroid extract was given in only 5 or possibly 6 of the cases.

This would appear to show that the thyroid administration had an important beneficial influence upon the cancerous growth. It must at once be admitted that thyroid extract has given the best results in cancer of breast.

In cancer of the viscera, such as intestine and uterus, it has so far given few, if any, results comparable to its successes in the inoperable cancers of the mammary gland. Nearly all observers are agreed that in cases where visceral metastases already exist thyroid extract, combined or not with oöphorectomy, has little or no influence upon the disease. The kind of case most suitable for thyroid treatment, as urged by Beatson and others, is where secondary growths occur only in the skin and lymphatic glands, but where visceral growths are absent.

Before attempting to explain something of the *modus operandi* of thyroid administration in carcinoma, I would like to refer to a number of cases of cancer which have apparently disappeared under the treatment of oöphorectomy and thyroid treatment, references to which will be appended.

1. The author's case.¹ Cancer of axilla, recurrence after operation with secondary nodules; duration of growth two and a half years; freedom from growth after thyroid treatment alone for eleven years.
2. Stanley Boyd's case.² Cancer of breast, secondary nodules, lymphatic glands; duration of disease eight years; freedom from disease three and a half years after oöphorectomy.
3. Herman's case.³ Cancer of breast, recurrent secondary nodules after operation, axillary glands; duration of disease nine years; freedom from disease after oöphorectomy and thyroid treatment three and a half years.
4. Cheyne's case.⁴ Cancer of breast, removed by operation, recurrence in axilla; duration of disease five years; oöphorectomy and thyroid treatment; apparently free from glands twelve months after.
5. Waterhouse's case.⁵ Cancer of breast, breast removed, recurrence in axillary and supraclavicular glands; duration of disease three and a quarter years; oöphorectomy and thyroid administration; disappearance of glands in four months and remains apparently well for eight months.
6. Beatson's case.⁶ Cancer of breast, recurrence in glands; duration of disease five years; oöphorectomy and thyroid administration; freedom from disease for two years.
- 7 and 8. Cheyne's two cases⁷ of cancer of the thyroid gland.

Writing to me on April 20th, 1909, Sir William Watson Cheyne says:

I have not written anything on the matter you speak of, but I did mention to Bashford two cases which, I feel sure, were malignant disease of the thyroid which got well after administration of thyroid extract.

It will thus be seen that, in all these recorded cases of apparent cure of cancer, thyroid extract was administered in all except Stanley Boyd's case. In three of them, the author's case and in Sir William Watson Cheyne's two cases of cancer of the thyroid gland, thyroid organo-therapy was used alone. These facts, together with the still larger number of cases in which the growth was undoubtedly

favourably modified and partially arrested by oöphorectomy and thyroid administration, compel one to the conclusion that in this form of organo-therapy we have a valuable means of treatment of cancer. In no sense can it be regarded as specific, but that it favourably influences the cancerous growth and enables the tissues to bring about a partial, and in some cases a complete, spontaneous cure, is highly probable. It must of course be understood that the author does not in any sense seek to supplant the well-recognized methods of radical removal by operation where this is possible. It would appear to be applicable to cases of inoperable carcinoma or recurrent cases of a limited extent.

I should, further, be prepared to advise thyroid administration as an adjunct to operative measures in operable carcinoma, hoping by such administration to prevent recurrence, and to enable the tissues to deal with minute foci of cancer which have escaped radical removal by surgical treatment.

The *modus operandi* of thyroid organo-therapy in carcinoma is a matter of pure speculation. Physiologists, however, have evolved so much of the action of thyroid secretion upon body metabolism that it is possible to suggest a plausible theory as to how this internal secretion or the administration of its animal extract by the mouth does influence the cellular growth of malignant disease.

Before attempting this I would like to refer to some of the facts concerning the life-history of cancer cells and their spontaneous disappearance which have been brought to our notice by Bashford, Handley, Bonney, and others.

There is now on record abundant clinical and experimental proof of the spontaneous cure of cancer. The clinical evidence is forthcoming in the authentic cases of complete spontaneous cure of mammary cancer published by Pearce Gould⁸ and Mackay,⁹ as well as the cases previously mentioned. Further support is given of this in the healing of cancerous ulcers, as shown by Pearce Gould in 1900; the occasional healing of fractures of bone due to cancerous growths; the disappearance of spinal metastases, as shown by Osler¹⁰; and the shrinkage of atrophic scirrhus. Careful observation has been made upon secondary nodules of the skin and it has now been proved beyond all doubt that many of these entirely disappear.

On the experimental side, Bashford and Murray,¹¹ at the Imperial Cancer Research Laboratories, have demonstrated clearly that spontaneous disappearance of cancer masses is by no means a rare occurrence in mice after artificial propagation. They have observed tumours at first manifesting rapid growth followed by cessation of growth and frequently by complete absorption.

Handley,¹² in a recent paper dealing with spontaneous cure of cancer in the human subject, enunciates the following law concerning cancerous growth:

Every aggregation of carcinoma cells has a definite life-cycle, and, after increasing in size for a varying period and at a varying rate, tends spontaneously to undergo degenerative and fibrotic changes. These changes extend from the centre of the mass centrifugally to its periphery, lead to its shrinkage, and terminate in the replacement of the aggregation of cancer cells by a fibrous scar.

In other words, the natural history of a cancer is one of centrifugal growth followed by centrifugal death.

This law, of course, is difficult of proof clinically, because, in the majority of cases, death of the patient takes place before the full life cycle of the cancer mass is complete. What is quite certain, however, is that the spontaneous cure of cancer is a local process and not a constitutional one. In this respect it resembles tubercle. In cancer, the natural cure beginning in the centre of the growth, rarely overtakes the centrifugal spread of the growth at the margin, although, in certain rare cases, the central degeneration and fibrosis is so rapid that it strangles the growing edge and leaves but a scar behind.

Bashford and Murray, in the experimental inoculation of cancer in mice, have made observations upon the life-history of cancer masses which are very much in accord with those of clinical observers. They have demonstrated remarkable fluctuations in the rate of growth of cancer masses, sudden exacerbations of rapid growth being followed by sudden cessations of growth to which they have given the names of positive and negative phase.

These fluctuations are probably due to one of two causes, namely, either to variation of suitability of the soil in which the cancer cells are growing, or to variations inherent within the cancer cells.

Both Handley and Bashford, the one working clinically and the other experimentally, have proved that cancer cells are obligatory parasites, and that they are dependent for their life upon the connective tissue cells in which they lie.

The rate of spread of the cancer is dependent partly upon the suitability of the soil or connective tissue just external to its advancing margin, and partly upon the inherent properties of cell proliferation within the cancer cells.

Victor Bonney,¹³ in his Hunterian Lecture, established a new important fact bearing upon the origin of cancer. It was that a local increase in the cellularity of the subepithelial connective tissues, accompanied also by a destruction of the elastic tissue, invariably precedes the appearance of carcinoma. This increased cellularity is due to a precedent chronic inflammation. If the chronic inflammation has progressed farther and has reached the stage of fibrosis and diminished cellularity, he finds that there is little risk of a carcinoma originating in the fibrosed area. The same increased cellularity of the connective tissue is seen at the margin of a growing cancer. It is therefore obvious that, as a cancer cell is but a parasite on the connective-tissue cell, any abnormal aggregation of the connective-tissue cells will only act as a body of hosts or caterers to the cancer cells, and therefore favour their growth.

Therefore, if by any means the proliferating, highly cellular connective tissue at the margin of the cancer mass can be converted into a fibrotic area, the rapidity of the cancer invasion is arrested and a negative phase of growth is obtained.

The above are a few of the facts known to us which govern the growth of cancerous masses. Handley has shown that fibrosis around cancerous masses does take place, not only in the connective tissue around the growth, but also in the lymphatic vessels leading away from it, and in this way the cancerous invasion is arrested.

Is there anything in these facts which can throw any light upon the probable action of thyroid extract in favouring the spontaneous cure of cancer in the human subject?

Physiologists have shown that thyroid secretion has a powerful action upon proteid katabolism as shown by increased nitrogenous excretion and loss of body weight. They have further shown that it lowers the blood pressure, causing increased circulation of lymph. This increased lymph circulation renders the blood more watery, and causes dehydration of the tissues.

These two physiological actions appear to me to offer some explanation of the beneficial action of thyroid extract in certain cases of cancer. The increased proteid katabolism might act in two ways. In the first place, it would shorten the life-history of the cancer cells by stimulating katabolic processes in them, and thereby favour degenerative processes and fibrosis of the central mass of the growth. In the second place, its influence upon the connective tissue immediately adjacent to the cancer focus is probably still more important. By its stimulation of proteid metabolism within the connective tissue cells, its acceleration of lymph flow and dehydration of the tissue, it would modify the increased cellularity of the subcancerous zone of connective tissue which, according to Bonney, is so favourable to cancerous invasion, by converting it into fibrotic connective tissue, and thereby arrest the centrifugal growth of the growing edge. By this dual action of quickened life-cycle of the cancer cells and fibrosis of the connective tissue around, a negative phase of the growth is obtained.

So much stress was laid by Handley and others upon the fortification of the soil, as represented by the connective tissue upon which the parasitic cancer cells depend for their nourishment, that they strongly advised that every attention should be paid to the general health of the individual; for example, they advocate open-air treatment and forced feeding as in tuberculosis, in order to give the tissues every chance of overcoming the cancer nodules.

In some such manner the administration of thyroid

extract may favourably influence carcinoma, and help to bring about spontaneous cure.

REFERENCES.

- ¹ BRITISH MEDICAL JOURNAL, 1901, p. 1145. ² *Ibid.*, 1900, p. 1162. ³ *Ibid.*, 1900, p. 1167. ⁴ *Ibid.*, 1900, p. 1162. ⁵ *Ibid.* ⁶ *Lancet*, 1897, p. 884. ⁷ Private letter. ⁸ *Clin. Soc. Trans.*, vol. xxxii, p. 272. ⁹ BRITISH MEDICAL JOURNAL, July 20th, 1907. ¹⁰ *Ibid.*, January 6th, 1906. ¹¹ *Science Progress*, Study of Cancer, No. 5, July, 1907. ¹² BRITISH MEDICAL JOURNAL, March 6th, 1909, p. 582. ¹³ *Lancet*, 1908.

A NOTE ON

"SENSORY TETANY," "VASOMOTOR TETANY,"
ACROPARAESTHESIA, AND RAYNAUD'S
SYMPTOMS.

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It must be admitted that the groups of symptoms described as tetany, acroparaesthesia, and Raynaud's disease overlap each other, and that cases occur in which one symptom-group becomes merged with one or both of the others. Tetany may be preceded or accompanied (or, in mild attacks, replaced) by numbness and tingling in the hands and feet (acroparaesthesia), and the motor symptoms of tetany may, I think, be regarded as the motor analogue of the sensory symptoms described as acroparaesthesia, and of the vasomotor phenomena known as Raynaud's disease. The latter symptom-group, according to this view, might almost be termed "vasomotor tetany," just as acroparaesthesia might be termed "sensory tetany." All these symptom-groups (or "clinical syndromes") seem to a great extent to resemble each other in regard to their etiology, as far, at least, as any causes have been recognized. Is it not possible that they are different manifestations of the same morbid states, the difference in the manifestation being due to age, sex, and individual peculiarities (idiosyncrasy) of the patient?

Thus, exposure to cold, a notorious exciting cause of Raynaud's phenomena and of acroparaesthesia, is likewise an occasional exciting cause of tetany. Conditions of malnutrition connected with rickets, diarrhoea (gastro-intestinal affections), and infectious diseases, are generally acknowledged to be causes of tetany in children. Malnutrition appears to favour conditions resembling Raynaud's disease in children and young adults. Congenital or acquired syphilis, malaria, and various infections often play a part in the production of Raynaud's phenomena both in adults and children. Operative removal of the thyroid gland (with the parathyroids) is a cause of (artificial) tetany, and it is probable that some temporary insufficiency of internal secretions plays a part in the "acrocyanosis" of young ("overgrown") subjects and in acroparaesthesia in elderly persons. Auto-intoxication of intestinal or gastric origin has probably an important share in the etiology, not only of tetany but likewise of acroparaesthesia and Raynaud's symptoms. A kind of auto-intoxication due to dilatation of the stomach is a well-recognized cause of tetany in adults, and F. Langmead has described cases of chronic intermittent or relapsing tetany in children associated with dilatation of the colon.*

To this latter point I wish specially to allude. Atonic dilatation of the colon is not rare in elderly persons with chronic constipation or with large, unformed, and infrequent stools of the "cloacal" kind. Do such persons suffer from symptoms in any way analogous to the chronic or intermittent tetany, described by Langmead, in children with dilatation of the colon? Probably these persons not rarely suffer from numbness, tingling, "pins and needles," sensations of heat, etc., in the hands (fingers) and feet, in fact from acroparaesthesia, which in such cases might perhaps justly be called mild chronic intermittent "sensory tetany."

* F. Langmead, *Trans. Clin. Soc. of London*, 1906, vol. xxxix, p. 48; also *Proc. Roy. Soc. Med.* (Section for Disease in Children), 1909, vol. ii, p. 218. This chronic tetany is apparently not met with in cases of congenital dilatation of the colon of the Hirschsprung type (megacolon), nor in cases of so-called "intestinal infantilism." I think, by the way, that I have once seen a very severe tremulous spastic condition of the extremities allied to acute tetany in a fatal case of acute or subacute ulcerative colitis in an adult.