

tion. That this is due to hæmolysis, however, is shown in various ways. As far back as 1843, Andral and Simon found the red corpuscles greatly reduced even during the early stages of the disease, a fact confirmed by Hayem and others. Roger Williams,⁹⁶ who refers to these authors, also states that "the red blood-corpuscles show signs of progressive deterioration and destruction. A marked diminution of the hæmoglobin was also shown to exist by Quinquaud, a fact confirmed by Chudowsky⁹⁷ after examining the blood of 51 cases, Donati⁹⁷ and others. Roger Williams says, moreover, that "a thousand grams of normal blood contain about 125 grams of this substance, whereas in cancer cases the amount often does not exceed 25 grams." He compares the condition to that which prevails in pernicious anæmia, which, as we will see, is due to hæmolysis. Finally, Kullmann⁹⁸ found recently that freshly-drawn blood of cancerous subjects contained a hæmolytic substance, and that it acquired especial activity when the cellular elements were present. That the only hæmolytic substance is auto-antitoxin, we have seen.

Other phenomena which are now misinterpreted are the serous effusions, the anasarca, etc. That they are due to general vasoconstriction is shown by the fact referred to by Roger Williams, that in cases that have run their natural course, "smallness of the heart, aorta and arterial trunks" is "observed post-mortem," and that as shown experimentally by Louis (1846), the "total quantity" of altered blood is "notably diminished." Considerable of their serum having passed into the subcutaneous tissues, the chest, etc., œdematous effusions occur. The cause of the excessive vasoconstriction becomes apparent also, when the direct action of the unusual quantity of the auto-antitoxin on muscular coats of the vessels is taken into account, as stated in the text. This effect should, however, also be manifest in the other muscles of the body. Klippel⁹⁹ observed that notwithstanding the wasting there was marked reflex hyperexcitability of the muscles. The excess of all three constituents of the auto-antitoxin is likewise shown by the paradoxical phenomenon recently observed by Sticker,¹⁰⁰ that when cancer had been successfully transplanted in dogs, these animals were immune to further inoculation. Indeed, the Cancer Research Commission also found recently, according to Bashford,¹⁰¹ that "an injection of healthy blood may protect mice against the subsequent inoculation of Jensen's tumor being successful." The reason for this becomes self-evident in view of the identity of the body's auto-protective agency, the auto-antitoxin that the blood contains.

That the adrenal should finally yield, under these conditions, is obvious. Nepveu¹⁰² found what lymphatics were present filled with detritus of various kinds, and epithelium. The morbid effects of the detritus are generally recognized. Eifer¹⁰³ compares the putrifying process to that which occurs in plants having parasitic excrescences. The roots of some of these, through various bacteria, including the bacillus amylobacter, become centers of infection which, owing to the cacodyle, give out a repulsive odor. In human cancer, the corresponding ulceration is due to pyogenic and other bacteria. Thus, Wlaëff,¹⁰⁴ found among others, the proteus septicus hominis and the bacillus coli communis. That these organisms enter the blood-stream was shown by

⁹⁶ Roger Williams: Edinburgh Med. Jour., June, 1897.

⁹⁷ Chudowsky: La méd. moderne, vol. vi, p. 151, 1895.

⁹⁷ Donati: Giorn. della r. Accad. di Med. d. Torino, June, 1901.

⁹⁸ Kullmann: Zeit. f. klin. Med., Bd. liii, S. 293, 1904.

⁹⁹ Klippel: Loc. cit.

¹⁰⁰ Sticker: Zeit. f. Krebsforschung, Bd. i, S. 413, 1904.

¹⁰¹ Bashford: Brit. Med. Jour., July 28, 1906.

¹⁰² Nepveu: Marseille-médical, Jan. 15, 1893.

¹⁰³ Eifer: Le correspondant médical, Aug., 1895.

¹⁰⁴ Wlaëff: Jour. de méd. de Paris, vol. xvi, pp. 255, 262, 1904.

Maragliano.¹⁰⁵ He examined the blood of 33 cancerous patients, and although the strictest antiseptic precautions were taken in each instance, he found staphylococci of various kinds in 9 instances. These were all cases in which ulceration had occurred, while no bacteria were found in the blood when such ulceration was absent. The general course of this additional morbid process is precisely that depicted by Roger Williams. "When ulceration sets in and the wound gets invaded by microbes," writes this observer, "the ordinary symptoms of septic infection may be added to those of the cancerous cachexia. Considering the putridity that characterizes these ulcerating cancers, especially when the uterus is the part affected, septic complications are remarkably rare; but no doubt in certain cases, they contribute their quota to the *ensemble* of symptoms. Hæmorrhages and suppurations further impoverish the blood and weaken the patient. At length, if not cut off by some intercurrent complication, death results from *asthenia*."

Treatment.—*Removal of the tumor* and of all contaminated glands or metastatic growths is followed by prompt recovery, even the cachectic phenomena disappearing in practically all cases. This procedure, when practicable without endangering the patient's life or producing unusually distressing deformities, is still, and rightly, too, *the method of choice*, until some non-surgical measure will have proven itself as reliable. Potent reasons urge, however, the need of such a measure: besides the desirability of avoiding mutilation, the impossibility to operate in some cases, the delay which dread of surgical procedures inspires, etc., there is the undeniable fact that removal of the growth serves but to defer its fatal effects in the vast majority of cases, an assertion but too clearly sustained by the ever-growing death-rate. The functions of the adrenal system not only opens a new field for the study of cancer but it suggests more encouraging lines of tentative treatment.

A cancer, in the light of the foregoing facts, is initiated, nourished and caused to grow by blood constituents which, as agents of the organism's auto-protective mechanism, should, in reality, have destroyed it from the start.* Owing to senility or other debilitating conditions, however, the defensive process, which requires an *excess* of auto-antitoxin, is inadequate; and mere nutrition, with mitotic proliferation of cells, *i.e.*, growth, results, because the blood's auto-antitoxin happens to be composed of the identical substances which, under normal conditions, nourish the tissues.* Our aim, therefore, should be to raise, if possible, the functional efficiency of the body's defensive

* *Author's conclusion.*

¹⁰⁵ Maragliano: Gazz. degli Osped., Jan. 13, 1901.

resources by means of agents which, by increasing markedly the functions of the adrenal system, augment correspondingly the proportion of auto-antitoxin in the blood and other body-fluids.* All the agents studied in the eighteenth and nineteenth chapters, and others not analyzed in the present work, are available to attain this end.* *Thyroid gland* occupies a prominent place among them, the most satisfactory being desiccated thyroid.

Thyroid extract was used in cancer as an adjunct to oöphorectomy, some years ago, by Beatson,¹⁰⁶ Stanley Boyd,¹⁰⁷ Dorland,¹⁰⁸ and others; but as removal of the ovaries might have accounted for the beneficial results noted, these reports can hardly be taken as guide. It was first used alone in cancer (and before Beatson) by Robert Bell,¹⁰⁹ with success. Recently,¹¹⁰ he stated that several of the recoveries were of over nine years' standing, although they included cases of mammary and uterine cancer. Page and Bishop¹¹¹ caused the entire disappearance of a carcinoma of the breast by the use of the gland alone, beginning with 3 grains (0.2 gm.) and increasing until 15 grains (1 gm.) were given daily. At the time of the report, two and one-half years later, was well, and no trace of the cancer could be discovered. Dennis¹¹² also obtained more benefit from the use of thyroid gland than from any other agent, while H. A. Beaver,¹¹³ in a desperate case of carcinoma (also recognized as such by Sir Francis Laking) nearing its end and attended by great suffering, obtained results "little short of marvelous." He states that "convalescence began immediately, so that by the end of January [the thyroid extract, 5 grains (0.33 gm.), quickly increased to 20 grains (1.33 gms.) daily, having been begun at the end of November] the patient was up and free from pain." The following October she "was quite well and was following an active life." E. Hughes Jones¹¹⁴ reports a cure of 11 years' standing in a woman aged 61 years, and R. H. Woods^{114a} the complete disappearance of a laryngeal cancer, under 3 grains of thyroid three times daily. He refers to Sir Charles Ball as having obtained successful results in 2 cases of inoperable cancerous lymphatic glands.

The prevailing empirical use of thyroid gland fails to afford the best results* and exposes the patient to complications,* for the following reasons: (1) The vigor with which large doses enhance oxygenation and catabolism through the adrenal system, not only in the body at large, but in the cancerous mass itself, entails an accumulation of waste-products in the lymphatics and blood-vessels beyond the excretory capacity of the kidneys. The indiscriminate use of such doses, therefore,

* Author's conclusion.

¹⁰⁶ Beatson: Brit. Med. Jour., June 6, 1896.

¹⁰⁷ Stanley Boyd: *Ibid.*, Oct. 2, 1897.

¹⁰⁸ Dorland: Therap. Gaz., May 15, 1899.

¹⁰⁹ Robert Bell: Trans. Brit. Gynec. Soc., vol. v, 1896.

¹¹⁰ Robert Bell: Brit. Med. Jour., Jan. 16, 1904.

¹¹¹ Page and Bishop: Lancet, May 28, 1898.

¹¹² Dennis: Jour. Amer. Med. Assoc., Oct. 19, 1901.

¹¹³ H. A. Beaver: Brit. Med. Jour., Feb. 1, 1902.

¹¹⁴ Jones: Brit. Med. Jour., Feb. 25, 1911.

^{114a} Woods: London letter, N. Y. Med. Jour., July, 1911.

exposes the patient to nephritis which may prove fatal; (2) the use of thyroid gland alone, by raising metabolic activity in the organism and in the growth, involves the corresponding consumption of the blood's sodium chloride and, though in a less degree, its alkaline salts.* If these are not replaced, the patient's vital functions become greatly depressed; and osmosis being deficient, he becomes readily vulnerable to intercurrent diseases, while the beneficial influence of the extract is thwarted, through the fact that the trypsin, the active agent of auto-antitoxin, loses its power in the absence of sodium chloride; (3) excessive, *i.e.*, still greater doses, by causing a correspondingly great quantity of thyroiodase to accumulate in the blood, soon influences the depressor nerve, and the functions of the patient's pituitary and thyroid bodies being inhibited, the stimulating action of the extract on the test-organ and adrenal center (through which its beneficial effects are produced) is prevented.*

The dose of desiccated thyroid should, therefore, be small to begin with: 1 grain (0.065 gm.) three times daily, in a subject of average health apart from the presence of the growth, this quantity being gradually increased by one grain (0.065 gm.) weekly, until 3 grains (0.2 gm.) are taken after each of the three meals—provided, however he does not complain of rheumatic pains (which indicate excessive metabolism), and his urine remains approximately normal, albuminuria being only regarded as abnormal when marked.*

To preserve the fluidity of the blood, facilitate the excretion of catabolic wastes and protect the kidneys by causing the specific gravity of the urine to remain low, a quart of some *mineral water*, such as Ballardvale, Londonderry Lithia, etc., should be drunk in the twenty-four hours.* This applies only, however, to patients whose diet is normal, *i.e.*, who ingest through its intermediary enough sodium chloride and alkaline salts to satisfy the needs of the organism.*

In fully developed cancer, the blood as a whole is deficient in *sodium chloride*. As the proteolytic activity of trypsin requires a fixed proportion of this salt—especially since it facilitates osmosis and tissue-metabolism—it should be given as an adjuvant to the thyroid extract.* Its use assumes additional

* Author's conclusion.

importance when the fever is marked, when the patient is on a milk diet, or when but little food is taken, since the latter must compensate the body for the sodium chloride excreted in the urine,* over one-half ounce (14 gms.) daily. The indications for its use are similar to those in febrile diseases,¹¹⁵ the quantity ingested being regulated by the degree of pyrexia.

In advanced cases, the renal functions are usually impaired. Sodium chloride under these conditions provokes oedema. It is also contraindicated if any form of oedema is already present. Plain or mineral water should then be used instead, as in the earlier stages of the disease.*

The fact that excessive doses of thyroid gland tend to aggravate the renal disorders to which cancerous subjects are liable is made self-evident not only by the well-known fact that it increases markedly the urea excretion, but also by several cases reported. The use of considerable pure or mineral water to insure adequate fluidity of the blood and to protect the kidneys is of considerable importance. In two of my cases it sufficed (without thyroid) to cause retrogression of the growth. In one of these, a breast cancer in the initial stages, about to be removed under the advice of two surgeons, there has been no recurrence, though six years have elapsed. The patient (æet. 74) faithfully continues drinking one quart of (still) mineral water daily. This points clearly to the importance of osmosis in the curative process.

The relationship between the functional efficiency of trypsin (the active proteolytic agent in auto-antitoxin) and sodium chloride is well-known to physiologists. Thus Halliburton¹¹⁶ states that pancreatic juice taken from a temporary fistula, contains 7.35 parts of sodium chloride in a thousand. As this is almost exactly the proportion in normal saline solution, trypsin, the active ferment in pancreatic juice, must require this proportion to exercise its proteolytic action most actively. This constitutes, therefore, an important feature in the treatment of cancer.

Again, Von den Velden¹¹⁷ has shown that free hydrochloric acid is absent in nearly all cases of gastric cancer. Osler¹¹⁸ states that "of 94 cases in which the contents were examined, in 84 free HCl was absent." This is not due to the local disease, for Moore, Roaf and Whitley¹¹⁹ found recently that in practically all cases of cancer, and wherever located, free hydrochloric acid is either absent from the gastric contents or greatly reduced in quantity. Now, as shown by the experiments of Voit and Cahn, "the chlorides present in the blood-plasma are the source of the acid."¹²⁰ Hammarsten¹²¹ also states that "there can be no doubt that the hydrochloric acid of the gastric juice originates from the chlorides of the blood." It is evident, such being the case, that the blood, as a whole, is deficient in sodium chloride. In the light of evidence previously adduced, therefore, the osmotic properties of the plasma and the activity of the adrenoxidase and trypsin are all impaired in cancer.

* Author's conclusion.

¹¹⁵ Cf. this volume, p. 1367.

¹¹⁶ Halliburton: Schäfer's "T. B. of Physiol.," vol. i, p. 77, 1898.

¹¹⁷ Von den Velden: Deut. Archiv f. klin. Med., Bd. xxiii, S. 369, 1879.

¹¹⁸ Osler: "Practice," sixth edition, p. 483, 1905.

¹¹⁹ Moore, Roaf and Whitley: Lancet, Dec. 16, 1905.

¹²⁰ Voit and Cahn: Cited by Moore: Schäfer's "T. B. of Physiol.," vol. i, p. 358, 1898.

¹²¹ Hammarsten: "T. B. of Physiol.-Chem.," fourth edition, p. 306, 1904.

I recommended the use of saline solution simultaneously with thyroid gland and the x-ray, in the first volume (January, 1903), also calling attention to the fact that "the curative process requires alkaline salts" to insure the full activity of the tryptic intraphagocytic digestion"—besides that of the cancerous cells carried on by the plasma's autolytic constituents. This in a measure accounts for the beneficial results obtained with sodium chloride alone by Rost.¹²² Freund¹²³ also found that the introduction of an alkaline fluid into arterial channels leading to the growth proved beneficial. But in view of the facts adduced above, it is evident that salt alone cannot prove curative.

Its contraindication in advanced cases is shown by the fact that Glosser and Frisbie¹²⁴ found experimentally that while a normal subject could ingest large quantities of sodium chloride without evil effect, cancer patients showed oedema when the chloride consumption was increased—a fact which they ascribe to the impairment of renal excretion. Indeed, oedema may occur in its various forms, as we have seen, when the cachectic period is reached—an indication that the kidneys are the seat of inflammatory lesions caused by the excessive functional activity imposed upon them and the local effects of toxic wastes.

X-ray and radium cause a rise of temperature and hyperæmia in the growth, thus causing the proteolytic activity of the auto-antitoxin (*i.e.*, its trypsin) in its blood.* The penetration of the x-rays is greater than that of radium; hence the great efficacy of the former. The frequent failures observed, however, are due to the paucity of auto-antitoxin in the blood.* Thyroid gland should be used simultaneously, therefore, in the manner indicated above.* *Cataphoresis* may likewise be advantageously employed in conjunction with thyroid gland and the use of fluids.

That the x-ray method alone may be effective both in sarcoma and epithelioma, has been shown by Morton, Allen, Pusey, Pfahler, Leonard, Skinner, Beck and others. Even here, breaking down of the tissues by the trypsin in the cancer is evidently the curative process. As noted by most clinicians, congestion is a prominent feature of the effect produced, the local temperature, as observed by Carl Beck,¹²⁵ being somewhat higher. As stated by Skinner,¹²⁶ moreover, "the effect of the x-ray light is due to a stimulation of the reparative functions of the tissues dependent on an inflammatory reaction," but *how* is this carried out? "Its destructive influence," continues Skinner, "is always exhibited on tissues which are low in vitality." The need of a destructive agent in the process asserts itself, however, and trypsin, we have seen, is present in large quantities in cancerous growths.

I advised the concomitant use of x-ray and thyroid gland over seven years ago.¹²⁷ Since then, Am Ende,¹²⁸ having used it in several instances, obtained beneficial results in two cases which, under x-rays alone, had failed. He mentions three cases which were proving rebel-

* Author's conclusion.

¹²² Rost: Alkaloidal Clinic, Aug., 1903.

¹²³ Freund: *Loc. cit.*

¹²⁴ Glosser and Frisbie: Jour. Amer. Med. Assoc., Feb. 24, 1906.

¹²⁵ Carl Beck: N. Y. Med. Jour., May 24, 1902.

¹²⁶ Skinner: Jour. Amer. Med. Assoc., Jan. 17, 1903.

¹²⁷ Sajous: Monthly Cyclo. of Pract. Med., May, 1903.

¹²⁸ Am Ende: Amer. Jour. of Surg., Aug., 1905.

lous to x-ray treatment and were given thyroid by R. T. Morris, in addition to the rays. "All three responded promptly," two being cured and the third improved. Another case of Morris's, an extensive recurrent carcinoma of the breast, also ended in cure under the combined treatment. Am Ende¹²⁹ recently reported seven cases in which recurrent growths were markedly reduced, some disappearing completely, by means of the combined use of a fluid extract of sheep's thyroid and radium or x-rays. In one instance, a case of adeno-carcinoma of the sigmoid flexure and rectum, diagnosed by laparotomy, and abandoned as lethal, normal health was restored.

In one case radium was used with thyroid by Am Ende, the result being "considerable constitutional betterment," besides the improvement of local symptoms. The action of radium is similar to that of x-rays, but as emphasized by Perthes¹³⁰ and Exner,¹³¹ its influence does not extend much beyond 2 or 3 centimeters from the surface. The influence of this on its therapeutic value is well shown by the following summary, by Catharine Macfarlane,¹³² of the results obtained by various clinicians: "13 rodent ulcers cured; 14 epidermoid cancers cured; 1 malignant wart cured; 11 cases of cancer of the œsophagus slightly improved; 1 sarcoma cured; 27 carcinomas unaffected; 1 malignant wart unaffected; 1 malignant mole unaffected; 1 rodent ulcer unaffected." Diminutive growths may be destroyed, therefore; thus, in 19 mice-cancers ranging from a pea to a bean in size, Apolant¹³³ obtained complete retrogression in 11, and reduction to mere traces in the rest. Morton, Lassar¹³⁴ and others have reported cures in human subjects, but, on the whole, radium is not as effective as the x-rays. Plimmer,¹³⁵ for example, tried radium in 17 cases, with but slight, if any, beneficial effect. In nearly every instance, however, the growth is said to have "blistered" or "reddened"—evidence to the effect that it provokes local hyperæmia—a well-known fact. When radium acts directly on ferments it soon destroys them, but Neuberg¹³⁶ has shown that when of two fragments of the same cancer, one is exposed to the action of radium and the other is not, the first will undergo disintegration twice as fast as the second. The wealth of these growths in trypsin, and the heat-energy supplied by the radium, account for this effect, as in the case of the x-ray. Indeed, here, there being no circulation of blood, the heat evoked by the radium alone becomes the energizing agent of the ferment. The use of cataphoresis, as practiced by Betton Massey, suggests itself as probably more effective than either the x-rays or radium, since it promotes disintegration of the growth, as does thyroid extract.

Thyroid gland is always indicated when the x-ray or radium is used, to prevent metastasis.* The proportion of auto-antitoxin in the blood and the tumor itself being increased, the cellular fragments and the soluble poisons liberated during the disintegration of the malignant tissues are themselves more perfectly broken down, thus reducing the chances of metastasis in proportion.*

* Author's conclusion.

¹²⁹ Am Ende: Jour. of Advanced Therap., Apr., 1907.

¹³⁰ Perthes: Verh. d. Deut. Gesellschaft f. Chir., Bd. ii, S. 398, 1904.

¹³¹ Exner: Deut. Zeit. f. Chir., Bd. lxxv, S. 379, 1904.

¹³² Catharine Macfarlane: Amer. Medicine, Apr., 1906.

¹³³ Apolant: Deut. med. Woch., Bd. xxx, S. 454, 1903.

¹³⁴ Lassar: Berl. klin. Woch., Bd. xli, S. 534, 1904.

¹³⁵ Plimmer: Lancet, Apr. 16, 1904.

¹³⁶ Neuberg: Zeit. f. Krebsforschung, Bd. ii, S. 171, 1904.

Allen, Coley¹³⁷ and other observers have found that metastasis occurred more frequently under the x-ray treatment than without it. This is readily explained by the fact that as the mass is being broken down, fragments and toxic juices (capable, we have seen, of causing metastasis in proximate or remote tissues) are freed into the lymph spaces in unusual quantities. The proportion of auto-antitoxin in the blood being in no way increased by the local treatment, the process of implantation or intrinsic inoculation is not antagonized. By powerfully stimulating the adrenal center, thyroid gland greatly increases not only the proteolytic activity of the blood and the proportion of phagocytes, but also that of the cancerous mass itself. The detached fragments, cells, and soluble poisons are thus, from the start, either reduced to the condition of benign wastes, or their activity as living cells or as bio-chemical elements is greatly diminished.

Epinephrin, supracapsulin or any other reliable active principle, in 1:1000 solution, painted or swabbed over the surface of the growth relieves pain, arrests hæmorrhage and even tends, by causing constriction of the vessels, to cause partial retrogression of the growth. Injection of 10 minims of the same solution into the tumors enhances further the latter effect; but the injections should be given under strict asepsis, and after carefully sterilizing the surface with a solution of the hydrogen peroxide.

The local effects of adrenalin in this connection was observed by C. Fiesinger,¹³⁸ who attributed them to its effect on vessels of the neoplasm. In cancer of the rectum, he found that painting twice daily with 30 to 100 drops of a 1:1000 solution of adrenalin in a tablespoonful of water decreased the rectitis, checked the discharge and brought about a temporary diminution of the growth. Mahu¹³⁹ had previously obtained prompt results by simply painting the growth with the 1:1000 solution. The neoplasm partially retrogressed; then remained stationary and free from pain or hæmorrhage, the patient being in apparently perfect health. In four other cases the results were also satisfactory. Berdier and Falabert¹⁴⁰ tried injections in advanced cases and found that they caused diminution of the tumor and of the adjoining glands, abolishing pain and increasing the patient's weight. The injections were made into the tumor or, when this was inaccessible, into the arm or over the organ involved. J. E. Rhodes¹⁴¹ reported a case of inoperable nasopharyngeal sarcoma in which the injection of adrenalin into the growth together with local swabbing and spraying caused marked reduction in size and alleviated the pain, though the patient's life was not prolonged. J. Price-Brown¹⁴² also found that adrenalin checked the circulation in sarcoma and lessened bleeding.

Adrenal gland, the glandula suprarenales sicca of the U. S. P., is of advantage in these cases to prevent anæmia by supplying the blood with the oxidizing constituent of the hæmoglobin.

* Author's conclusion.

¹³⁷ Coley: Amer. Jour. Med. Sci., Mar., 1906.

¹³⁸ Fiesinger: Journal des Praticiens, Apr. 23, 1903.

¹³⁹ Mahu: La Presse Médicale, Apr. 4, 1903.

¹⁴⁰ Berdier and Falabert: Semana Medica; Jour. Amer. Med. Assoc., Mar. 25, 1905.

¹⁴¹ Rhodes: Jour. Amer. Med. Assoc., Aug. 11, 1906.

¹⁴² Price-Brown: Med. Record, Oct. 6, 1906.

Three grains three times daily with *iron*, preferably Blaud's pill, 1 grain, prolong life by retarding the cancerous cachexia.

The usefulness of adrenal gland in this connection was illustrated by one of my cases of advanced uterine cancer in which life was considerably prolonged, improvement of the patient's condition having become manifest soon after the use of the gland had been begun. It seemed also to prevent severe pain, doubtless by causing constriction of the arterioles, thus reducing the local hyperæmia and swelling. The patient died, in fact, without knowing that she had suffered from cancer.

The simultaneous use of *radium*, *thyroid gland* and *adrenal gland*, the two latter in the above-mentioned doses, improves the likelihood of recovery beyond those offered by radium alone.

The creation of the Radium Institute in Paris has rendered possible a closer study of the technique, and, as a result, the curative value of radium has shown itself to be greater than had been generally supposed. Wickham,¹⁴³ a clinician of the first order, has observed remarkable results in a variety of cases, including epithelioma not only of the surface, but of such organs as the breast. By means of appropriate metal shields he regulates the activity of the radium and employs the *beta* and *gamma* rays only for deep-seated growths. On the other hand, my own experience with opotherapy has amply demonstrated their helpful influence in malignant growths.

Various organic extracts, including *testicular juice*, *lymph-gland juice*, an extract of *ram's testicles*, and *thymus extract* have been tried. None of these substances, however, are endowed with the specific properties of thyroid extract. Even *adrenalin* is useless given internally, since it is oxidized before it reaches the tumor at all. *Iodine* and the *iodides* have been extolled by various observers. The fact that thyroidase is an organic compound of iodine points to the iodides, especially sodium iodide, as a substitute when thyroid gland is not well borne.*

Mikhailoff considers potassium iodide a specific in cancer. In a preliminary communication¹⁴⁴ he announced that he had obtained favorable results with this treatment. He recently reported a case of cancer of the œsophagus treated by potassium iodide with marked success. Many other remedies have been tried, but their enumeration would be out of place in this work.

Although the various "cancer sera" or "antitoxins" are composed of the constituents of auto-antitoxin, the quantity introduced is inadequate to produce more than fleeting effects. A continuous exogenous supply is necessary to replace the auto-antitoxin formed under the influence of adrenal stimulants.*

More efficacious are the various *toxins*, especially *Coley's* mixed toxins of erysipelas and bacillus prodigiosus. They also produce disintegration of the growth by stimulating the adrenal

* Author's conclusion.

¹⁴³ Brit. Jour. of Dermatology, July, 1909.

¹⁴⁴ Mikhailoff: Roussky Vrach, Dec., 1906.

center, and through it, therefore, the formation of auto-antitoxin.* Toxins are only efficacious in sarcoma, however, because this variety of cancer occurs usually in subjects who are young, and whose adrenal system is more vigorous; and because the greater vascular supply of the growths themselves renders them more vulnerable to the disintegrating action of the auto-antitoxin.* For carcinoma, however, the action of toxins on the adrenal center is inadequate and less efficacious than that of thyroid extract.* Their value is sufficient, however, to warrant their use in sarcoma, especially with x-rays, which distinctly enhance their effects. (See also p. 757, vol. i.)

The treatment by auto-antitoxin was introduced by Richet and Héricourt, of Paris, in 1895, who obtained encouraging results in cancer patients, by injecting blood from animals previously injected with an extract of cancer tissue. Jensen, in 1901, cured cancerous mice by injections of blood from rabbits previously injected, a result also obtained by Clowes and Baeslack¹⁴⁵ and others. Leyden and Blumenthal¹⁴⁶ reported positive results both in dogs and man by means of serum derived from goats treated months with injections of carcinoma. Gaylord, Clowes and Baeslack¹⁴⁷ then showed that the serum of mice treated with immunizing serum was capable of causing the disappearance of small tumors and checking the growth of the larger ones. A number of sera have been introduced by as many investigators, all giving results similar to those recited above. Tuffier¹⁴⁸ found that any one of them injected in turn into a cancer patient causes retrogression of the lesions to a certain extent and improvement of the clinical picture, but these beneficial effects become gradually less. At times, no beneficial effect is obtained, as in cases reported by D'Arcy Power.¹⁴⁹ Analysis of these cases in the light of my views, however, shows that the curative process had started, and identifies the nature of the process; thus he complains that it caused an *inflammation in the growths*. The disease progressed to a fatal issue while the injections were being given.

The treatment by toxins, which, like thyroid, causes adrenal stimulation, may be illustrated by the treatment of inoperable sarcoma by mixed toxins of erysipelas and bacillus prodigiosus as practiced by W. B. Coley, of New York, since 1892, the use of the first-named toxin having been suggested by the inadvertent cure of a severe case of very malignant sarcoma, which had recurred four times, by two attacks of erysipelas. In a recent paper to which the reader is referred,¹⁵⁰ Coley gives statistics of a large number of cases treated by himself and by other surgeons, showing a large proportion of recoveries (the patients being from 3 to 13 years old). That the curative process is due to great increase of auto-antitoxin in the blood, is shown by the fact that results are linked with the temperature ratio. "The dose should be gradually increased," writes Coley, "until a chill occurs (one-half to two hours after injection), followed by a temperature of 101° to 103°

* Author's conclusion.

¹⁴⁵ Clowes and Baeslack: Med. News, Nov. 18, 1905.

¹⁴⁶ Leyden and Blumenthal: Deut. med. Woch., June 11, 1903.

¹⁴⁷ Gaylord, Clowes and Baeslack: Med. News, Jan. 14, 1905.

¹⁴⁸ Tuffier: Presse médicale, vol. xii, p. 27, 1905.

¹⁴⁹ D'Arcy Power: Brit. Med. Jour., Feb. 6, 1904.

¹⁵⁰ Coley: Loc. cit.

or 104° F." (some cases mentioned reaching 105°), "the destructive process in the growth being manifested in most cases by "breaking down"—precisely the effect produced by thyroid extract and trypsin. Schmittle¹⁵⁴ observed that the temperature kept high after the injection of toxins unless brought down by an antipyretic. The use of toxins is not devoid of risk, however. Marmaduke Shield¹⁵⁵ observed a case which, though there was "undoubted and apparent disappearance of the growth," a fact which he ascribes "purely to inflammatory action," ended in death, the autopsy showing the signs of "general pyæmia."

In sarcoma the x-ray method is of but little value. Coley gave it a careful trial in 68 cases, and obtained very unsatisfactory results, and prompt recurrence. When, however, the toxins were injected in addition to the x-ray treatment, the effect was very marked, recovery occurring in two out of six instances. This indicates that it is *through the blood* that the curative influence is exerted—as it is when the thyroid is used.

The local application on the ulcerated surface of a 1 per 1000 solution of *adrenalin* relieves pain and controls hæmorrhage. The latter effect is also encouraged by thyroid extract, since by stimulating the adrenal center it increases the proportion of fibrin ferment (adrenoxidase) in the blood, and facilitates coagulation.* To asepticize the ulceration and control the factor, *formalin* in a 2-per-cent. solution is quite effective when the dressing is changed every six hours.

Fiessinger¹⁵⁶ found that 30 to 100 drops of a 1 to 1000 solution of adrenalin injected with a tablespoonful of water, gave a marked relief in rectal cancer. Mahu¹⁵⁷ used it in the manner indicated above in seven cases, including mammary and rectal cancers. The growths partially retrogressed and remained stationary without causing discomfort. Berdier and de Falabert¹⁵⁸ obtained similar effects by injecting the solution into the growth or in the adjacent tissues. Powell¹⁵⁹ found formalin capable not only of causing the effects mentioned in the text, but also that it tended to promote destruction of the malignant mass. Beneficial effects have also been reported by other observers.

It is important to realize that all these measures have—as with many others tried—proven curative in a very small proportion of cases.

Prophylaxis.—In the light of the foregoing facts, the prevention of cancer would reduce itself to measures calculated to increase the efficiency of the adrenal system.* The "cancer facies," *i.e.*, a peculiar pallor sometimes observed in subjects who subsequently develop cancer (as well as in many who do not), assumes importance if there is a clearly defined

* *Author's conclusion.*

¹⁵⁴ Schmittle: New Orleans Med. and Surg. Jour., Dec., 1895.

¹⁵⁵ Marmaduke Shield: Brit. Med. Jour., Jan. 23, 1897.

¹⁵⁶ Fiessinger: Jour. des praticiens, Apr. 25, 1903.

¹⁵⁷ Mahu: Presse médicale, vol. x, p. 281, 1903.

¹⁵⁸ Berdier and de Falabert: Semana Medica; Jour. Amer. Med. Assoc., Mar. 25, 1905.

¹⁵⁹ Powell: Brit. Med. Jour., May 30, 1903.

hereditary predisposition—a fact which means that congenital hypoactivity of the adrenal system may favor the liability* and if the patient is past middle life. The presence of a mole, nævi, papillomata, scars, warts, lingual sores or fissures from the presence of a pipe stem or sharp teeth, chronic uterine disorders, fibromata, chronic ulcers, patches of eczema, etc., may, as we have seen, render a given area liable to the development of cancer. Such lesions, even in a person who shows no hereditary predisposition, when combined with pallor, sallowness, or any condition of the skin which points to deficiency of blood in its capillaries, are prone to malignancy if irritated.*

In most cases, the cause of the pallor, etc., is due to low vascular tonus, the great vessels of the splanchnic area being engorged, while the peripheral vessels are ischemic, due, in turn, to hypoactivity of the adrenal system.* Here, *strychnine* is of exceeding value, because it activates both the vasomotor and adrenal centers, in doses of $\frac{1}{40}$ grain (0.0016 gm.) increased to $\frac{1}{30}$ grain (0.0021 gm.) taken after meals. The *hydrochlorate of quinine*, 2 grains (0.13 gm.), when taken during a meal, does not cause gastric disorders and is likewise effective. If adynamia be present, *thyroid gland* in small doses, 1 grain (0.06 gm.), may either be given alone or with *quinine* or *Mariani coca wine*.* A course of the *iodides*, beginning with 5 grains (0.03 gm.) three times daily in a large glassful of water, increasing the dose gradually to 10 grains (0.06 gm.), is also useful, especially if given with the *strychnine*.*

All these remedies, and others studied in the department on Pharmacodynamics, raise the blood-pressure more or less, and a greater volume of blood enriched with auto-antitoxin and phagocytes being caused to circulate in the cutaneous and other capillaries, the normal defensive resources are raised to their normal level.* This means that adventitious cellular elements in exposed areas are promptly catabolized by the auto-antitoxin, that the detritus is promptly removed by phagocytes, and that the local process of repair is carried on normally.*

In the case of internal cancers, apart from regions that are directly examinable, the larynx, the uterine os, etc., the dan-

* *Author's conclusion.*

ger signals are scant and opportunities for prophylactic measures are few. That gall-stones predispose to primary carcinoma of the gall-bladder is well known; hæmorrhages from the stomach, rectum or vagina, in prematurely aged persons, are also familiar precursors of local cancers, especially if associated with emaciation. They may be looked upon, therefore, with sufficient mistrust to warrant prophylactic measures. In these cases, either of the agents previously recommended may be used. *Thyroid gland*, 2 grains (0.13 gm.), and *Squibb's extract of ergot*, 1 grain (0.065 gm.), each in a capsule, taken jointly during meals, are also very effective. The thyroid gland causes a prompt increase of fibrin ferment (adrenoxidase) and prevents the hæmorrhage, while the ergot, by inducing a rise of blood-pressure, causes the exposed area to receive an excess of blood rich in auto-antitoxin.*

The deeper and greater organs, when predisposed to cancer, afford no reliable preliminary clue. Emaciation occurs when a growth is too small to give evidence of its presence, but we are no longer dealing with prophylaxis here, and the measures to be carried out are those indicated for a developed cancer, those indicated under Treatment.

Out-of-door exercise is of paramount value in the preventive treatment of cancer, to increase the vigor of the circulation in the peripheral vessels and enhance general metabolic activity. Laziness, physical and mental, predisposes to cancer, by promoting circulatory torpor and recession of the blood from the periphery.* The use of alcoholic drinks, whiskey, brandy, etc., is also pernicious, since the alcohol becomes oxidized at the expense of the blood, thus impairing its antitoxic activity.* Coffee and tea, on the other hand, are beneficial, being vasomotor stimulants.* The free use of *pure water* is in itself a protective measure, since it preserves the blood's normal fluidity.*

Such cases require watching. In one of mine, now under observation since October, 1901, a frail woman in whom the symptoms of mammary cancer were sufficiently developed to warrant operation (advised by two surgeons), the tumor was caused to recede by thyroid extract. If she allows her health to run down, however, ominous signs appear, and she must resume treatment. Arsenic is harmful in her case, a fact accounted for by the depressing influence of this agent on the adrenal system. Indeed it counteracts directly the effects of thyroid extract. An exception to the use of thyroid—or, in fact, of any drug—has asserted

* Author's conclusion.

itself in one of my cases, *i.e.*, one of hepatic cancer. While benefited by the copious use of mineral water (Ballardvale, one quart daily) through the fact doubtless that the fluidity of the blood and of the bile facilitated the elimination of detritus, any drug, even in small doses, would at once aggravate his condition. Drugs, taken against my advice, promptly caused death. My diagnosis of hepatic cancer proved true *post mortem*.

On the whole, the prophylaxis of cancer—which includes the prevention of recurrence after removal of the growth—entails as fundamental principle the preservation of the organism's normal defensive activity through the adrenal mechanism.*

This intimate relationship with Immunity, and which, as previously stated, I was first to point out and explain, in 1903, has since been sustained by considerable experimental evidence. Gaylord, Clowes, and Baeslack¹⁰⁰ found an immune body in the blood of mice which had recovered spontaneously from experimental adeno-carcinoma, while Clowes¹⁰¹ afforded evidence to the effect that "mice which have recovered from cancer possess an active immunity against further inoculation." Ehrlich¹⁰² found (1) that a rat or mouse in which inoculation had caused cancer, a second inoculation failed to do so; and (2) that when tumor material too weak to cause a growth was injected into animals, the majority of them became subsequently, *i.e.*, in from one to two weeks, immune to inoculation. To explain his first observation, Ehrlich states that the specific nutrient materials were used by the first growth—a pure supposition. From my viewpoint, the reaction of the adrenal system to destroy the tumor and its detritus, loaded the blood with antibodies, *i.e.*, auto-antitoxin, and the material of the second inoculation was promptly destroyed. Ehrlich explains his second and most valuable observation by his side-chain theory. I have shown, however, that the latter is not tenable as far as the tissue-cells being the original source of the antibodies is concerned, and that he has failed to establish the identity of these antibodies because he has neglected the ductless glands. Such obscurity does not prevail with the adrenal system as the basis of reasoning: Ehrlich produced immunity against cancer because the injected material increased powerfully the functional activity of the adrenal system, and thus caused an accumulation of auto-antitoxin of sufficient magnitude, in from one to two weeks, to protect the animal against the further inoculation—precisely as he had in his first experiment.

* Author's conclusion.

¹⁰⁰ Gaylord, Clowes, and Baeslack: *Loc. cit.*

¹⁰¹ Clowes: *Loc. cit.*

¹⁰² Ehrlich: *Loc. cit.*