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An Address

ON

**ACUTE CONSTITUTIONAL SYMPTOMS
DUE TO RADIATIONS.***

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It is a familiar truism that any kind of treatment powerful for good may under certain conditions, such as excessive dose or undue susceptibility of the organism, do harm; this danger is much more imminent when the drug, method, or operation is of recent introduction and its potentialities and limitations as yet imperfectly explored. X rays and radium are very powerful agents and have a wide field of application in the treatment of disease; as a form of energy they exert a profound effect on metabolism, acting in either a stimulating or destructive manner according to the conditions of their dosage and the state of the body. This, of course, is obvious in the various skin lesions—dermatitis, growths, and burns—from which radiologists and their patients may suffer. The selective action of irradiations on the tissues, or the sensitiveness to rays of the various cells of the body, is important both from the point of view of treatment and of the ill effects that may thus be induced. The destructive action exerted by radiations on the blood-forming organs, especially on lymphoid tissue, has attracted much attention recently on account of the unfortunate fatalities among x-ray and radium workers.

Experimental investigations of the changes in the lymphocytes have been carried out by Mottram, S. Russ, Leitch, Lazarus-Barlow, Hess, Unger and Steiner, and others; and G. E. Pfahler⁴⁵ has quite recently reviewed this subject. The chronic blood changes and ill health that may occur in x-ray and radium workers are now generally recognized and guarded against. The action of radium on the nervous tissues has been much investigated since 1903 by Danysz, Obersteiner, Alquier, and Faure-Beaulieu. In 1911 Horsley and Finzi applied filtered radium rays directly to the brain, and stated that the nerve cells were unaltered, but that from damage to the blood vessels haemorrhages occurred. In 1922 Morowoka and Mott, from histological examination of the brains of animals whose heads had been exposed to a large amount of radium, attached importance to the protective action of the skull. Pendergrass, Hayman, Houser, and Rambo, employing various methods of acting on the brain by radium, found that the nerve cells were first destroyed and then underwent autolysis. Bone is the most resistant tissue of the body to radiations, but Regaud⁴⁶ found that it may show necrotic changes from x rays without any concomitant damage to the skin. The remarkable sensitiveness of the mucous membrane of the small intestine in dogs to x rays has been shown by Warren and Whipple, who found that the lymphoid tissue in Peyer's patches was much less susceptible; Lazarus-Barlow's experiments also showed that the mucosa of the small intestine of cats, rabbits, rats, and frogs was damaged by the gamma rays of radium. Warren and Whipple ascribe the grave constitutional symptoms produced in dogs by exposure of the abdomen to enormous doses of x rays to the lesion of the small intestine.

ACUTE CONSTITUTIONAL SYMPTOMS DUE TO RADIATIONS.

Synonyms: Roentgen-ray intoxication; Radio-toxaemia; Mal des rayons; Disease of penetrating rays; Röntgenkatarrh.

Discussion of the acute constitutional symptoms due to radiations is appropriate at the present time when radiology is so rapidly advancing and measures of protection have

rightly been seriously taken in hand. An account of this grave ill effect of radiations necessarily entails some reference to the commoner and more or less immediate disturbance which presents resemblances in kind and indeed is difficult to distinguish from the mild type of constitutional symptoms, but is less severe and very possibly due to a different cause.

The use of x rays in medical practice, which began in 1896, was soon followed by reports of the ill effects; the skin lesions were noted in the same year, and in 1897 D. Walsh first drew attention to the constitutional effects; he recorded two such cases in x-ray workers, in one of whom the symptoms disappeared when the abdomen was shielded by lead. Since then a considerable literature has grown up on this accident, which, although in the past much rarer, and, as a rule, less serious than the skin lesions, especially carcinoma (of which according to Ledoux-Lebard there have been 100 victims among radiologists), is worthy of attention. These acute reactions are becoming more frequent with the use of massive doses of deep penetrating rays which by the "cross-fire" method of administration do not cause skin lesions. Thus, to take what it may be hoped is an extreme example: Rosenthal treated eleven cases of myeloid leukaemia by penetrating irradiations in three directions, and as a result all the patients had severe constitutional disturbance coming on soon after the treatment; three of the patients died, but the eight that survived were remarkably improved for six to ten months. Bécélère,⁴⁷ who quotes this paper, has had verbal information of similar cases in Germany. Inquiry from my radiological friends shows that cases of this severity are rare. Acute constitutional symptoms from the use of radium appear to be both less often noted and, when they occur, shorter and less severe than those induced by x rays (Regaud,⁴⁸ Desjardins). Captain A. E. Hayward Pinch of the Radium Institute allows me to quote him to the effect that he has no knowledge of acute constitutional symptoms in radium workers, but he refers to a real systemic disturbance due to auto-intoxication and characterized by slight fever and general malaise in patients, especially those with lymphosarcoma, after deep radium therapy.⁴⁹ According to Bowing, mild reactions, such as malaise, anorexia, nausea, and occasional vomiting, are usually disregarded at the Mayo Clinic, but when a severe reaction occurs the radium treatment is usually omitted for two to three days.

Onset of Symptoms.

According to the reports available, the acute constitutional symptoms may come on within a few hours or be delayed for as long as twenty days. The duration of the latent period is generally stated to vary inversely as the intensity and the length of the exposures; and usually a long latent period is followed by mild symptoms, whereas the shorter the latent period the more severe the constitutional disturbance. But there are apparent exceptions to these rules. Variation in the onset of acute constitutional symptoms may possibly be explained in the following way: that the immediate or rapid onset, on the same or next day, of symptoms such as malaise, lassitude, nausea, vomiting, headache, and giddiness, is due to a cause different from that responsible for the graver constitutional disturbance which does not come on until later.

It may be convenient to refer here to the causation of the early symptoms. Three possible factors may be mentioned: (1) Mallet and Coliez incriminate the ozone in the air of x-ray rooms; though this has been widely recognized it can hardly be the sole factor, for Hayward Pinch mentions deep radium therapy, which does not involve an ionized atmosphere, as a cause of similar symptoms. (2) Schrumpf-Pierron believes that high electrical charging of the patient's body is responsible and that putting the patient to earth obviates this inconvenience; this explanation is also rendered incomplete by the symptoms seen after deep radium therapy. (3) M. Giraud, G. Giraud, and Parès⁵⁰ argue

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that the early symptoms are due to haemoclastic shock caused by destruction of leucocytes; in intensive x-ray treatment lasting for hours this would seem to be highly probable. Possibly all three of these factors may in different circumstances be operative. That auto-suggestion is responsible seems unlikely. It is reasonable to believe that the later or grave constitutional symptoms, which are due to metabolic changes in the cells of the body as a result of radiation, may sometimes be superimposed on, and so appear to be continuous with, the primary disturbance; this would be more likely to follow intensive and prolonged x-ray exposures, after which both the early and the grave constitutional symptoms are prone to occur sooner and more frequently. Cases in which the early and the late disturbances have both been noted in the same patient after an irradiation have seldom been reported; Dr. R. Knox has told me of a case manifesting both groups of symptoms with an interval separating them.

The acute constitutional symptoms are usually the same in kind, though their degree naturally differs, so that two groups—the severe and the mild—are recognizable. The symptoms are toxæmic and mainly gastro-intestinal and cardio-vascular, well-marked motor impairment of the nervous system being exceptional. The most severe cases present nausea, uncontrollable vomiting, offensive diarrhoea with the passage of blood, abdominal pain and distension, fever, which in a fatal case under my observation reached 104° F., restlessness, profound prostration, progressive cardiac failure, small rapid pulse, and dyspnoea. In one of Rosenthal's cases, fatal on the sixth day after exposure, flaccid paralysis of the lower limbs involving the bladder and the diaphragm appeared on the day before death. In fatal cases death usually occurs within a few days of the onset, thus recalling the experimental results obtained by Warren and Whipple, who exposed the abdomens of dogs to high doses of x rays from a medium hard Coolidge tube and found that the animals nearly always died on the fourth day after exposure.

Fortunately the constitutional symptoms are more often mild than severe. In these circumstances the symptoms are malaise, lassitude, loss of appetite, nausea, and occasionally vomiting, the syndrome being compared by Bécélère⁸ to seasickness. The symptoms resemble those already mentioned as coming on shortly after the exposure to x rays and ascribed to ozone. The question arises whether or not a distinction between these latter bad effects, ascribed to the highly ionized atmosphere of x-ray rooms on the one hand, and mild constitutional symptoms due to the action of x rays on the tissues on the other hand, can be based on the interval that elapses between the x-ray exposure and the appearance of ill effects. It seems doubtful if such a distinction can be maintained, and it must therefore be admitted that it may be difficult to be certain of the exact nature of comparatively mild symptoms appearing soon after radiations.

For the following details of an example of mild constitutional disturbance in a radiologist, which appear to show that the symptoms depend on radiation of the intestines and had a definite latent period of nearly three weeks, I am much indebted to Dr. A. E. Barclay.

Starting x-ray work in 1904, he always did a great deal of screening under bad conditions and without an apron; since 1914 his private work was carried on with a Coolidge tube in the usual half-open box. In 1916, after a very prolonged course of screen examinations, often with a minimum of protection, he suffered, while working in France, from several persistent attacks of diarrhoea—sudden rushes of watery and offensive stools lasting for one or two days, gradually passing off and then coming on again. There was no nausea, and, except on one or two occasions, discomfort was absent; indeed, apart from the diarrhoea and loss in weight, he was in perfect health. Subsequently diarrhoea with much offensive flatus recurred at intervals, very occasionally being severe and accompanied by nausea and vomiting. Usually the attack started with malaise, which passed off when the bowels acted, the first motion being solid, followed about a quarter of an hour later by a liquid stool, and then by six to eight evacuations of an extremely watery character; in a few hours he would feel that all the fluid had been got rid of and he knew that the attack was at an end. On the few occasions on which casts were detected there was a burning sensation about the anus, but this disappeared completely with the evacuation of the cast. After one attack with nausea for an hour or two only and no other discomfort his weight dropped one stone, but in two weeks' time, although some minor attacks intervened, this was regained. In 1921, as the attacks were getting worse, x-ray work was given up for four months, and three weeks from the date of the last exposure the symptoms disappeared. On returning to work an attack followed after an interval of twenty days, a cast two inches long being passed; and on eight other occasions an interval of eighteen to twenty days between exposure and an attack was definitely established. The most efficient means of protection was then adopted in the form of an apron made of fairly thin lead rubber, covering the front and

back of the body. Since then he has been free from attacks, except on two occasions after examinations conducted in other x-ray departments.

Site of the Exposure in Human Cases.

Many of the instances of acute constitutional disturbance have occurred after intense radiation of the abdomen—for example, for leukaemia (Rosenthal) or for inoperable malignant disease; and according to Desjardins radiation of the upper part of the abdomen is particularly likely to be followed by acute symptoms. The exposure of large tumours far from the abdomen may also cause constitutional symptoms. It appears that radiation of the pelvis and the contained organs may reach the abdominal contents. At any rate it is admitted that constitutional symptoms, usually of a mild character, may follow radiation of the pelvis for uterine carcinoma and fibromyomas, and metrorrhagia (Bécélère⁸; Chambacher and Descoust; von Franz; Knox). From his wide experience Bécélère considers that the occurrence of serious lesions should be avoided by good technique and accurate dosage, but he refers to ulceration of the rectum and pelvic colon following very strong radiations by cross-firing. Similar damage to the rectum may occur in the radium treatment of carcinoma of the cervix uteri unless care is taken. In connexion with the view that the grave constitutional reactions depend on damage to the mucosa of the small intestine, attention may be called to Grunkrant's caution that, as in x-ray treatment of the pelvic organs the small intestine is traversed by the rays, the genupectoral or Trendelenburg position, whereby the small bowel, is removed out of the field, may with advantage be employed.

The post-mortem appearances in fatal cases of acute constitutional symptoms in man have not often been recorded. In Rosenthal's three fatal cases no morbid lesion was reported; but in von Franz's case the necropsy, performed by Orth, revealed severe ulceration of the small intestine and the colon. Bécélère's⁸ cases of perforation and stenosis following ulceration of the rectum and pelvic colon after intensive x-ray treatment of the uterus, have already been mentioned.

Cause of Acute Constitutional Symptoms.

The cause of the acute constitutional symptoms has naturally attracted much interest and some speculation. The following views may be mentioned: (1) The bad ventilation of the x-ray rooms leading to contamination of the atmosphere with gases such as ozone and nitrous acid, produced by the x-ray apparatus. (2) That the symptoms are due to acidosis. (3) That from destruction of cells and liberation of their protein a condition of anaphylaxis results. (4) That the protein products due to cellular destruction produce an acute intoxication.

1. Pfahler¹⁴ suggested that the acute constitutional symptoms depend on contamination of the air in ill-ventilated x-ray rooms by gases produced by high-tension currents. Konrich found that with ozone present in the proportion of 0.5 mg. per c.c.m. of air nausea, headache, irritable cough, and exhaustion rapidly occur and that chronic blood changes follow. But the suggestion that nitrous acid in excess in x-ray rooms is responsible for the bad effects is combated by Guthmann on the grounds that in chemical laboratories nitrous acid is present in ten times the amount that it is in x-ray rooms and yet chemists do not suffer in the way that x-ray workers do. That noxious gases must be regarded as a source of danger especially to the x-ray worker is obvious, but the bad effects ascribed to the highly ionized atmosphere of badly ventilated x-ray rooms are apparently not exactly identical with the severe constitutional symptoms, for they do not include diarrhoea or evidence of acute enteritis, and they come on very soon after x-ray exposure. Too much stress, however, must not be laid on the difference in the symptoms. Mallet and Coliez have drawn a sharp distinction between (a) the early or primary disturbance occurring the same day or the following day after irradiation, and due to the inhalation of contaminated air, and (b) the delayed onset of secondary symptoms caused by destruction of the cells of the body. The immediate effects are relatively transient, passing off in forty-eight hours, and are somewhat obviated by the administration of morphine during the exposure. Confusion may arise when an x-ray worker or patient suffering from the chronic effects (blood changes) of noxious gases is attacked by acute constitutional symptoms, which would then appear to be merely an exacerbation of the existing ill health, whereas it is in reality a second intoxication of a different character, though no doubt its incidence is favoured by the previous debility and lowered resistance. A good reason why the acute constitutional disturbance cannot be ascribed, at any rate solely, to the action of the contaminated

atmosphere of the x -ray rooms is that similar acute constitutional symptoms may be produced by radium. This has not only been noted clinically, but has been produced experimentally by the intravenous injection of the active deposit of radium into dogs by Theis and Bagg, who reported general constitutional disturbance, nausea, vomiting, severe diarrhoea, and intestinal lesions. As radium and x rays are practically identical in their effects on the tissues of the body and on biochemical processes, it follows that the acute constitutional symptoms are due to the action of the x rays rather than to concomitant gas poisoning. These considerations, of course, in no way minimize the bad effects of gases generated in ill-ventilated x -ray rooms, especially the abundant production of ozone from the frequency of brush discharges due to the exposed condition of high-tension wires²⁰; and it may not be out of place to insist on the recommendations of the "X-ray and Radium Protection Committee,"²¹ and the need for good ventilation, sunlight, and extraction fans in x -ray rooms.

2. Lange put forward the view that acidosis, local or general, due to cellular destruction and metabolism is the responsible factor, but did not give any chemical evidence, such as analysis of the expired air or of the blood, to support this hypothesis; Denis, Martin, and Aldrich were inclined to accept Lange's view. Case states that at Battle Creek Sanatorium the tests for acidosis have proved negative.*

3. The suggestion that the acute constitutional symptoms are anaphylactic in nature appears to depend on (a) the knowledge that as the result of x -ray exposures the cells of the body, especially the lymphocytes, are destroyed with liberation of their protein, and (b) reported cases of patients whose tolerance to x rays appears to become progressively less, so that eventually acute constitutional symptoms occur.

Bergonié in 1916, believing that a tissue once damaged by x rays remains for a long, if not for all, time sensitive in a greater or less degree, spoke of this state as one of indirect or physical anaphylaxis and much the same as chemical anaphylaxis; C. Richet, the author of the much used word "anaphylaxis," expressed his agreement that although the exciting cause was physical the process at work was chemical. More recently de Courmelles has carried on this interpretation and describes the condition of x ray sensitization as more than anaphylactic shock, and as a physico-chemical rather than a purely chemical change. M. Giraud, G. Giraud, and Parès²² record a case of myeloid leukaemia, in which tolerance to x rays was good until after the remarkably long period of five years' treatment, when it diminished, so that after each exposure to x rays, which were made less as time went on, there followed a transient crisis, described as anaphylactic in nature, of intense nausea, copious vomiting, general malaise, dyspnoea, and vertigo, and associated with a fall of the leucocyte count and of the blood pressure. These crises were associated with the haemoclastic signs described by Vidal and his collaborators, but there was not any evidence of hepatic insufficiency, and the responsible cause was regarded as sensitization of the body by proteins liberated by the destruction of leucocytes by x rays. These authors state that radiologists may die after a holiday, during which sensitization supervenes from accumulation of antibodies; but no statistical proof is given of this rather startling statement. Cases certainly occur in which tolerance to radiation, at first good, subsequently fails, so that acute constitutional symptoms occur; I have personal knowledge of a patient who after tolerating x -ray exposures without any ill effect for some time had two severe attacks, at five months' interval, after successive x -ray exposures of the abdomen, the second of which proved fatal. Emil Beck refers to patients who after one attack of radio-toxaemia are just as susceptible to another attack, if not more so than they were at first. Cases showing this development of hypersensitiveness to radiations are so exceptional that it is not unreasonable to suggest that some cause other than true anaphylaxis is responsible for the phenomenon. An obvious objection to the hypothesis of anaphylaxis is that both experimentally and clinically the acute symptoms occur after the first exposure to x rays; this was seen in the three patients long ago described by Edsall and Pemberton. From experimental x -ray exposures of dogs Hall and Whipple definitely opposed the existence of x -ray anaphylaxis or hypersensitiveness; they indeed found that there was some evidence of slightly increased tolerance to a second exposure—a conclusion endorsed by L. Loeb, who

mentions the possibility that a new race of cells, which are resistant to x rays, may arise.

4. The view that protein products from the cellular destruction caused by radiations give rise to an acute intoxication has received wide support. That cellular destruction follows exposure to x rays is too well known to require further mention, and numerous observations point to the increased protein metabolism, as shown by the increased amount of protein derivatives in the urine. Hall and Whipple, in their experimental production of acute Roentgen intoxication in dogs, found increased excretion of nitrogen in the urine and a rise of the non-protein nitrogen in the blood before the fatal intoxication. Edsall and Pemberton believed that this process chiefly occurred in tissues rich in nucleo-proteins, and that the products of this form of protein are toxic, difficult to metabolize and to excrete, and that the resulting intoxication does not depend on renal damage caused by the x rays. They also suggested that x rays have a cytolytic action in virtue of their stimulating effect on autolytic ferments. The source of the toxic bodies would thus appear to be mainly the lymphoid tissues and the white cells in the blood. But there is also clinical evidence that acute constitutional symptoms follow the destruction of cells in tumours, such as large growths in the neck and breast; this is supported by the knowledge that toxic symptoms may be associated with necrosis and autolysis of new growths and inflammatory formations, especially gummas, as is shown in the striking condition of syphilitic fever. Loeper considers that protein products from metastases of gastric carcinoma after x -ray exposures enter the circulation and are the cause of the constitutional symptoms in x ray intoxication.

Recently Whipple and Warren have provided experimental evidence that a primary lesion in the mucous membrane of the small intestine produced by x rays may be entirely responsible for a non-specific intoxication—that is, one not due to any constant bacterial infection—which resembles in some respects that described by Whipple²³ in intestinal obstruction and due to a proteose; but there are differences, for in proteose poisoning the coagulation time of the blood is prolonged, whereas after x -ray exposures it is shortened (Stephan; Feissly; Pagniez, Ravina, and Solomon; Joltrain and Benard; Giraud, Giraud, and Parès²⁴)—an effect ascribed to liberation of thrombokinase from the destroyed leucocytes. Warren and Whipple's view is based, as already mentioned, on experiments on dogs in which massive doses of x rays to the thorax, the abdomen being adequately shielded, caused almost complete disappearance of the red bone marrow from the ribs, but no constitutional symptoms, thus proving that changes in the bone marrow and also in the intrathoracic lymphatic glands were not responsible for the acute symptoms in these dogs. Similar x -ray exposures of the abdomen, the thorax being protected, constantly caused acute destructive changes in the mucous membrane of the small intestine and severe constitutional symptoms; the histological changes were not those of an intense inflammatory reaction such as might be expected from bacterial invasion. The occurrence of intestinal lesions after x -ray exposures had previously been noted (by Regaud, Nogier, and Lacassagne in dogs; by Albers-Schönberg, Oberndorfer, and Fromme in guinea-pigs and mice); and Denis, Martin, and Aldrich regarded these lesions in rabbits as the result rather than the cause of the x ray intoxication. In 1918 H. E. Schmidt expressed his opinion that damage to the gastro-intestinal mucosa was the cause of the acute constitutional symptoms in man. Warren and Whipple's observations went to prove that the mucosa of the small intestine was specially sensitive to x rays, and that the lesion was not a secondary change, as Denis, Martin, and Aldrich contended. They also found that the cell ferments in the intestinal mucosa were much altered and that the rate of the autolysis of the secretory epithelium of Lieberkühn's crypts was much increased, more so than in the epithelium covering the villi.

There has been considerable discussion about the part played by intracellular enzymes in the cellular destruction following radiations; it has been stated that radiations activate the autolytic ferments and so cause destruction of the cells (Edsall and Pemberton, Packard). The results of researches on the influence of radiations on ferment action are discordant. Henri and Mayer found that the prolonged action of radium destroyed emulsin and trypsin; but Willcock, while confirming this observation for trypsin, pepsin, and ptyalin, showed that tyrosinase was not affected, and suggested that oxidases, being less specialized than digestive ferments, were not influenced by radium. Neuberg considered that radiation

* Since this address was delivered Ross Golden (*Arch. Int. Med.*, Chicago, 1922, xxx, 629) has published observations on four patients with Roentgen-ray sickness and three experimental dogs showing that there is not any evidence of acidosis.

destroyed the intracellular ferments with the exception of the autolytic enzymes. According to Richards, short exposures increase whereas long exposures inhibit or destroy ferment activity, and this view is endorsed by Peterson and Saelhof. Other observers report that radiations have no effect on enzymes (Richter and Gerhartz; H. A. Colwell).

Assuming that the enzymes are not destroyed, Pendergrass, Hayman, Houser and Rambo, in a recent paper dealing fully with the results of experimental exposure of the brain to radium, give an attractive explanation of the toxæmia which was thus produced in animals. They believe that the radiations lead to death of the nucleus and then of the nerve cells which undergo autolysis by the action of the intracellular ferments, and that the lecithin-lipoids, so abundant in the brain, are thus broken up into choline and neurine—the responsible causes of the toxæmia. They argue that the products of cellular autolysis must vary with the character of the tissues acted on by the radiations; thus when the intestines, as in Warren and Whipple's experiments, or the uterus, are exposed to radiations the resulting toxæmia will be proteolytic in nature and due to protein bodies, and so differ from the autolytic products of nerve cells described by them. Dr. H. A. Colwell, from independent investigations, has arrived at much the same conclusion, which though unpublished he kindly allows me to quote—namely, that the primary action of rays is to produce a disturbance of the colloidal equilibrium of the cell, the injured elements of which are then acted upon by the intracellular enzymes.

To sum up: it seems probable that the acute constitutional symptoms are due to flooding of the circulation with proteins liberated by the destruction of cells. Experimentally it has been proved that this can certainly be due to damage to the mucous membrane of the small intestine; clinical evidence is also compatible with this view, but also shows that destruction of cells in other parts of the body, such as large growths in the neck and in the mammary region, may be followed by acute constitutional symptoms.

Further Determining Factors in the Occurrence of Acute Constitutional Symptoms.

As acute constitutional symptoms are comparatively rare in ordinary practice, the question naturally arises on what further factors their occurrence depends. From Warren and Whipple's experiments, in which high doses of α rays over the abdomen constantly produced these grave symptoms in dogs, it appears that the dosage is a factor of great importance. The factor of the dosage has been generally recognized by α -ray workers, and is being more abundantly proved by the reactions seen after the Erlangen treatment. Two other possible factors may be mentioned: (1) Edsall and Pemberton argued that persons already in a toxic condition are more prone than healthy individuals to manifest acute constitutional symptoms, because they are already embarrassed in dealing with the intoxication and, if to this strain is added the metabolic labour of dealing with the complete decomposition of a large amount of broken-down tissue products, the metabolism may collapse, and in consequence signs of severe intoxication appear. This is not, as shown by Warren and Whipple's experiments, an essential condition, and as many of the patients exposed to abdominal radiation are in a toxic state but do not manifest the symptoms of acute constitutional disturbance, it cannot be regarded as a very far-reaching factor. (2) The patient's idiosyncrasy, rather vague as this influence may be, must be considered as a factor that may possibly favour the development of an acute reaction. This question has been much debated, and it appears that while there is naturally a certain amount of variation in the susceptibility of individuals to radiations and that reactions of different kinds are occasionally seen, an extreme degree of sensitiveness, comparable to other idiosyncrasies, is very rare.

Treatment is first and foremost preventive; to avoid the early transient disturbance the α -ray rooms should be properly ventilated. The avoidance of the grave constitutional symptoms mainly depends on care in the technique and dosage, but other factors may play a part, and the state of the organism must be taken into account. Proust, Mallet, and Coliez mention a red blood count below four millions and a low blood pressure as indications that α -ray therapy should be conducted with great caution. In order to avoid toxæmia Beck practises surgical exposure and surgical removal of as much as possible of the growth, and then treatment by α rays or radium of the remainder of the tumour in the open wound. In this way any discharge from the radiated tissue passes into the dressing instead of into the circulation and toxæmia

is minimized. Another advantage is that a smaller dose of radiations is required than in the ordinary method of treating deep-seated tumours. In 100 cases thus treated he had not had any death from toxæmia, whereas with the usual method four of his patients had died from toxæmia.

It is to be hoped that Auer and Witherbee's⁶⁴ experimental protection of the skin of rabbits against the harmful effects of α rays by the previous injection of horse serum may be applied to protect the deeper tissues of man against radiations. But before this is done further work is necessary; it is not yet known if the sensitization produced by horse serum increases the resistance of the cells of malignant growths to radiations.

When the symptoms have appeared, elimination of the toxic proteins may be assisted by diuresis, and for this purpose plenty of fluids should be given by the mouth. In conformity with his unproved hypothesis that the responsible factor is acidosis, Lange advocated the administration of sodium bicarbonate, and reported benefit from its use before and after radiation.

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