transient painful swellings, as stings had done in previous years, but to no general symptoms. A fortnight later he was attacked by a swarm of bees while walking along a road, and was again stung on the face 4 or 5 times; he ran away, and in about 2 minutes collapsed and died. Artificial respiration, continued for an hour, was without effect.

Case 5.—This patient, a man aged 55, owned and lived on a sisal farm which chanced to have a particularly large bee population. For 20 years he had been stung at least a dozen times a year with no ill effects beyond slight and passing local swellings. A sudden change for the worse took place in this state of affairs. One day, while playing bridge on a veranda, he was stung in the leg. He felt very ill, collapsed in 2 or 3 minutes, was unconscious, cyanosed, and pulseless for 10 minutes, passed water and motions, and struggled violently on coming to. Twenty minutes later he was well enough to drive himself home in his car. During the next 9 months he had 10 more similar attacks on being stung; each attack was said to be more severe than the previous one. The last attack but one followed a sting on the forehead; the patient walked into the house, collapsed in half a minute, and was cyanosed and pulseless for 10 minutes. Two hypodermic injections of strychnine were given and the pulse slowly returned; while still unconscious the patient passed water and motions, as always happened in these attacks, had a violent rigor, and dripped with perspiration. He was placed on a couch and slept for 4 or 5 hours, waking up perfectly well. The eleventh and last attack followed a sting in the neck, and proved fatal in about 15 minutes.

Discussion

It seems reasonable to assume that in Case 4 the patient was sensitized or rendered hypersensitive to bee venom by the 4 or 5 stings he received a fortnight before his death. But in Case 5 there is, unfortunately, nothing to show why the patient suddenly became hypersensitive to bee venom 9 months before he died, after having been quite insensitive to it for 20 years. The sensitization in Case 4 was specific; in Case 5 it may have been specific, but the possibility of non-specific sensitization to bee venom (Foulkes, 1939; Bray, 1934; Oriel, 1936) should not be overlooked.

An explanation of sudden death occurring after wasp- or bee-stings often met with in medical literature (Dyke, 1941; Barber, 1941; Cummins, 1939) is that the sting has chanced to puncture a vein in the dermis, so that some of the venom enters the circulation direct instead of being fixed and destroyed by the skin. The cases detailed above lend no

struck a vein in the dermis. In fact, this theory of venepuncture is superfluous. A better explanation of such sudden deaths can be given in terms of idiosyncrasy, hypersensitiveness, allergy, or anaphylaxis. If the signs and symptoms observed in severe or fatal cases of bee-stings are compared with those recorded (Bray, 1934; Lamson, 1924) in severe or fatal cases of serum disease, as in the accompanying Table, the two are seen to be nearly identical, and death in each case can properly be set down to anaphylactic shock.

Summary

The frequency of bee-stings in Kenya Colony is noted. Three cases of multiple bee-stings with recovery and 2 fatal cases are recorded.

The suggestion that fatal cases occur when the sting penetrates a vein is discredited.

It is argued that death in fatal cases of bee-stings is due to anaphylactic shock, as it is in fatal cases of serum disease.

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INDIRECT RADIOTHERAPY*

BY

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Radiotherapy as ordinarily practised exerts a local destructive effect. Indirect radiotherapy produces good results by its effects on function, especially that of the sympathetic and glandular systems. Radiations act very differently on cells *in vitro* and *in vivo*. Their effects cannot be measured solely by the morphological changes which they produce; other less-known modifications have a great field of usefulness in treatment.

Cardiovascular Disorders

In *arterial hypertension*, which Vaquez showed to be due to excessive development of the suprarenal glands, irradiation of the suprarenal capsules has been widely practised since 1913. Generally speaking, in chronic constitutional hypertension with no evidence of nephritis or of any other assignable cause, irradiation does not reduce the blood pressure any more readily than do the simpler methods of rest and diet. On the other hand, it often greatly relieves the functional symptoms, such as headache, vertigo, spasm, and muscae volitantes. Similar results are obtainable with high-frequency current. Moreover, exacerbations of hypertension are quickly controlled by irradiation of the suprarenals, though the underlying condition is unaltered. The dosage is comparatively slight, and no change in the suprarenal tissues has been observed at necropsy. These apparently contradictory observations may be explained by Bard's differentiation of arterial hypertension into several varieties. Some of these he suggests are compensatory either for some known disorder like nephritis or for an unknown disturbance. To reverse the physiological changes, the cause, whatever it is, must be treated. On the other hand, hypertension due to a derangement of the mechanism controlling arterio-constriction is amenable to suprarenal irradiation.

Thrombo-arteritis obliterans falls into two classes: local, due to compression, embolism, or localized thrombosis; and general. Local forms may respond to various other kinds of treatment but never to radiotherapy; in the general group, cases which develop rapidly from infection and septicaemia do not respond to irradiation, but chronic and subacute cases

Severe Bee-stings	Severe Serum Disease
Restlessness, apprehension Unconsciousness	Restlessness, apprehension Vision completely lost Unconsciousness
General Symptoms	
Erythema, pallor Urticaria Giant urticaria Itching, local or general Numbness, tingling Generalized burning pain Sweating	Erythema, pallor Urticaria Large confluent wheals Itching, local or general Numbness, tingling Generalized sudden pain
Muscular System	
Uncontrollable twitching Muscular spasms Convulsions, rigor Transient paralyses of eye, pharynx, limbs Intense weakness	Twitching of face Spasms of arms and legs Severe convulsions, tonic and clonic Opisthotonos Dilatation of pupils
Heart and Lungs	
Anginal pain in chest Heart failure Heart beating after cessation of respiration Cyanosis Acute dyspnoea Cheyne-Stokes breathing Crowing respiration Respiratory failure	Pain in chest Heart failure, syncope Heart beating for 3 to 15 minutes after cessation of respiration Cyanosis Acute dyspnoea, choking cough Typical attack of asthma Respiratory failure
Digestive Tract	
Violent diarrhoea and vomiting Loss of sphincter control Inability to swallow	Violent diarrhoea and vomiting Loss of sphincter control

support to this notion. In Case 5 one cannot believe that the bees should have missed the veins a dozen times a year for 20 years and in the ensuing 9 months punctured them 11 times in succession. And in Cases 1, 2, and 3 it is hard to imagine that not one out of so many hundreds of stings should have

* Translation abridged for publication.

—for instance, in young or old persons or in diabetics—can be notably improved and sometimes clinically cured. The results depend on the stage at which the lesions are treated. The best time for treatment is naturally when the symptoms are still at their mildest and the vascular system can respond to irradiation of the sympathetic nervous system.

Thrombo-arteritis generally attacks a large artery and always sets up a reflex vasoconstriction of the collateral circulation. The aim of treatment is not to restore circulation in the artery, for this cannot yet be done; it is to suppress the vasoconstrictor reflex and so allow the collateral circulation to continue to supply blood to the limb. Accordingly, irradiation is applied to the suprarenal area—i.e., between D 10 and L 2; to the periaortic plexus, which surrounds the iliac arteries; and to Scarpa's triangles and the popliteal spaces ("carrefours arteriels"). The pain nearly always disappears, though on the night after the first or second treatment the symptoms are aggravated. When the pain is associated with gangrene, radiotherapy is only palliative. On the other hand, irradiation acts on the vasomotor symptoms almost at once. The patient often notices during the first treatment a feeling of heat, which can be felt by the hand; the limb can also be much more readily warmed in bed or by an external source of heat. The oscillometric index hardly ever varies to correspond, and the claudication is reduced but never entirely banished.

On trophic disorders and gangrene, irradiation has an undeniable but an unreliable effect. The least favourable indications are torpid wounds and chronic gangrene in old persons. The results have, of course, to be assessed with discrimination. In sphacelus and gangrene the pain due to the arteritis is relieved, and frequently the gangrenous process is arrested and a drainage channel is formed; sometimes the condition may even clear up. In other cases the local pain due to the gangrene persists in spite of a strong impression that the process has been stopped or slowed. The limb will then have to be amputated; but the patient's condition may be much improved, as the operation can be performed under better conditions, sparing a larger portion of the limb.

Arteritis in old patients, especially when the calcified arteries are visible in the radiograph, gives the least encouraging results. Juvenile arteritis is the most favourable indication. In diabetic patients the most important requirement is to reduce the blood sugar. The prognosis for moist gangrene is always very bad.

Irradiation of the sympathetic also produces several effects apart from the changes in the pathological condition. In Raynaud's disease it has little action by itself but reinforces the action of diathermy. When the cervical region is included it will often clear up vasomotor symptoms due to trauma in which disturbance of the sympathetic balance produces vasoconstriction. Possibly it might have an equally beneficial effect on pathological vasodilatation, as in erythromelalgia: its action is polyvalent, and it produces always the effect opposite to that of the pathological condition.

There exists in most cardiac disorders a functional element which is susceptible to irradiation. Several workers, including Pruche and Bienvenue, give a small exciting dose to an area of the cervico-dorsal spine at the level of the stellate ganglion. The results are a toning-up of the myocardium, reinforcement of the action of digitalis, and diminution of the tachycardia; but no definite conclusion can yet be drawn from the relatively small number of cases treated.

Dermatoses

Gouin and Bienvenue found that the irradiation of primary warts would clear up secondary warts at a considerable distance. They suggest that the rays excite the nerve endings of the skin to produce, by way of the afferent fibres of the vegetative system, sympathetic reflex actions which modify the lesion. This theory does not seem to apply to the particular instance of warts, but has been borne out by their results in other skin disorders. Since 1924 they have treated Wilson's lichen planus by superficial irradiation of the interscapular region, the rays being centred on D 4 for lesions of the upper and on D 10 for lesions of the lower limbs. They give only one application, and if it fails they do not try another for three weeks. The evening after the treatment the pruritus is often aggravated for two or three hours, but by the next morning

it completely disappears; during the next three or four weeks the papules flake off and disappear. Pautrier of Strasbourg uses a method which he calls medullary radiotherapy: he employs thicker filtration, a higher kilovoltage, and a larger dosage, given in two parts at intervals of three days. Broadly speaking, Gouin and Bienvenue limit the action to the cutaneous afferent fibres, while Pautrier's aim is to irradiate the roots or medullary ganglia of the visceral sympathetic system. His method is perhaps better adapted to cases of longer standing.

In supramalleolar erythrocyanosis Gouin and Bienvenue use either spinal or axial irradiation. When the skin disorder is associated with others, such as dysmenorrhoea or acne, they irradiate the arterial carrefours; if the menstrual trouble is predominant, they begin by spinal irradiation and irradiate the carrefours three weeks afterwards. The duration of chilblains can be considerably shortened by irradiation of the carrefours, and they may be prevented from recurring. If they have ulcerated before cicatrizing they will secrete copiously. They clear up a fortnight after irradiation.

Acrocyanosis is treated by irradiation of the carrefours, or, if this does not succeed, of the interscapular region or the lumbar curve as the case may require. In long-standing cases the suprarenal area should also be irradiated. Cure is hardly ever quite complete. In eczema with lichen formation the methods both of Gouin and of Pautrier have succeeded brilliantly. During the war of 1914-18 Delherm obtained remarkable results in causalgia by irradiating the various spinal sympathetic branches and the vascular carrefours. Schulze's acroparaesthesia has also been cured or much improved by the same method; and it will often mitigate pain in amputation stumps.

In diabetes mellitus indirect irradiation brings about two interesting effects. Desplats of Lille reported that it reduced the glycosuria; and in some cases irradiation is followed by a sudden rise in excreted sugar followed by a gradual fall which lasts a long time. In severe diabetes with emaciation, on the other hand, irradiation, when it has any effect at all, makes matters worse. Irradiation of the pituitary gland will often render insulin-resistant patients sensitive. Obviously it acts on the sugar-regulating function of the anterior lobe, but in order to be effective the hormone of this lobe must have adrenaline associated with it.

In menstrual troubles not due to any lesion or anatomical abnormality, irradiation of the carrefours gives interesting results. The disorder of ovarian function responsible for these troubles often coincides with facial acne, pruritus, or eczema of the genital region. Desplats, irradiating the suprarenal area instead of the lumbar curve, obtained good results alike in this class of disorder and in those associated with the physiological or surgical menopause. Usually a single treatment is sufficient; if it is not, a second and sometimes a third are given, at intervals of eight days.

Asthma has been treated by irradiating various portals of entry, including the thorax, the thorax and spleen, the pituitary, the pancreatic region, and the bulb. The exponents of these different techniques adduce their successes to confirm a variety of aetiological theories; the benefit is probably due to a non-specific protein shock.

In Graves's disease associated with sympathicotonia, an inverted oculo-cardiac reflex, and a basal metabolism only slightly above normal or even a little below it, neither irradiation of the thyroid nor surgery gives any relief; the only effective treatment is irradiation of the suprarenal area.

Mechanism of Action

As the very small dosage produces no anatomical change it must modify function. The glandular secretions have been shown to be increased or reduced by it—a somewhat disturbing observation, for histologists (except for the doubtful results of R. Isaacs) have never yet been able to demonstrate that x rays stimulate cellular metabolism. On the other hand, radiations are known to modify, *in vivo* and *in vitro*, the fluid media of the body. Certain organic compounds—e.g., cholesterol, the fats, and amidin—are split up by hydrolysis; and the viscosity of the colloids is increased, according to dosage, up to the point of gelation. Richard Seydherhelm, by injecting previously withdrawn blood, could prevent or cure the anaemia

induced in an animal by the injection of saponin. It seems permissible to assume that these chemical changes, and perhaps also others as yet unknown, affect the glandular system without producing any appreciable anatomical alteration. They naturally vary according to the nature and degree of the disorder.

Through all the portals of entry employed the rays have access to the sympathetic nervous system. Radiotherapy therefore can modify the function of the sympathetic, and also of its perivascular plexuses, in various ways according to the dosage and the degree of excitability of the nerves. Gouin and Bienvenue produced by irradiation of the sympathetic the same reactions in the blood and the same clinical and therapeutic phenomena as Leriche produced by surgery. Moreover, besides the endocrine glands, which secrete their products into the blood, P. Masson has demonstrated the existence of endocrine tissues which secrete directly into the nerves. These two actions, humoral and nervous, proceed together. For instance, adrenaline acts by exciting the sympathetic nerves. Comparative anatomy and embryology show the close association of chromaffin with the sympathetic, and experimental physiology shows the close interaction of certain hormonal influences with corresponding neural factors—"sympatheticoglandular synergy." It is therefore easily conceivable that radiotherapy applied to the sympathetic and glandular systems may excite modifications which produce the beneficial effects that have been noted. As yet no one knows why or how it restores a disturbed balance by acting on that phase of the reciprocal vegetative function which happens to be impaired. This and many other difficult questions remain to be answered, and the answers will be as interesting as they are valuable.

TREATMENT OF PHOSPHORUS BURNS

BY

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A notable increase in the incidence of phosphorus burns must be expected under war conditions, and the article by E. W. Godding and H. E. F. Notton in the *Journal* of April 4 (p. 433) is therefore timely and useful. There are several points in this article which deserve further comment. It should be stated that the "official treatment" which they critically examine has been based on the practice gradually established through long clinical experience within the chemical industry and is the result of careful observation over many cases. These authors are under a misapprehension on one minor issue, as they assume that the copper sulphate treatment is designed chemically and completely to destroy the phosphorus particles left in the affected area after the preliminary washing. This is not the primary object, which is rather to destroy minute particles and to make obvious, by blackening, the larger pieces so that they can be removed mechanically. There is no present clinical evidence that the concentrations, both of alkali and of copper sulphate, suggested "officially" are inadequate, and indeed the extant case histories indicate that they are well chosen. Godding and Notton have done well, however, to stress that the alkaline treatment must be thorough, and the importance of this feature is borne out by my practical experience. A novel problem associated with present conditions is the satisfactory treatment of phosphorus burns under field or Service conditions. Here the practice found good enough in industry would often be difficult to apply with the requisite speed, and a satisfactory field dressing would be a valuable contribution to the casualty services. The powders suggested by Godding and Notton may prove of value in this connexion, and should certainly be given a thorough trial on human cases; it may be possible to get the requisite experience industrially. One further caution is necessary: Godding and Notton experimented with material from S.I.P. (self-

igniting phosphorus) grenades, and this is not strictly comparable to the phosphorus as encountered in industry, though the effects may reasonably be assumed to be similar. The following notes on the treatment of phosphorus burns may be of interest:

Characteristics of the Burns

Burns caused by phosphorus have long been recognized as particularly severe and troublesome lesions. They have these characteristics: (a) the initial pain is severe; (b) a greyish area is produced almost immediately at the site of the lesion, and blistering is rare; (c) sepsis is particularly apt to ensue; (d) healing is prolonged, and the resulting scar is often thin and atrophic. During the past ten years I have had the opportunity of studying burns arising from a variety of chemical irritants and corrosives. Generally, the severity of burns is proportionate to the chemical nature of the causative agent, and may be placed in the following order: (1) hydrofluoric acid, (2) phosphorus, (3) sodium sulphide, (4) caustic soda, (5) sulphuric and other acids.

Method of Treatment

The essential factor in the treatment of all chemical burns is the immediate flooding of the area affected with water or sodium bicarbonate solution. It is necessary to organize an adequate first-aid service for this purpose. Buckets of water, running water, eye-wash bottles, and, in special cases, baths must be instantly available. Experience has indicated that immediate flooding with water and *prolonged soaking in warm sodium bicarbonate solution* is the essential feature in treatment.

Altogether 65 cases of burns caused by phosphorus have been observed, the records of which are set out in the accompanying Tables. (In every case the time taken to heal is recorded as a period which elapsed before the employee was able to return to normal work without any dressings.) Several methods

Cases treated with Sodium Bicarbonate, Copper Sulphate, Acriflavine Emulsion (1/1,000), and Boroseptic Ointment

Age	Date of Burn	No. of Burns	Area Affected	Degree	Total Size (sq. in.)	Days Absent from Work	Days taken to Heal	Comments
22	24/1/39	4	Fingers	3	2½	Nil	30	
34	14/3/39	1	R. forearm	1	8	"	17	
34	14/5/39	1	Eyelids, face	2, 3	9	Hosp. 28	17	
29	29/6/39	1	Heel	3	6	30	22	
46	8/6/39	1	Ankle	3	4	16	10	
27	9/7/39	4	Wrist, fingers	2	2	Nil	30	
36	14/7/39	4	Neck, chest	2, 3	5½	"	49	Skin eruption with acriflavine
36	14/10/39	1	Forearm	3	1½	Hosp. 81	79	Sensitive thin scar. Skin eruption with acriflavine
42	26/10/39	1	Finger	3	1½	Nil	19	
41	12/11/39	1	"	3	½	"	17	
42	16/11/39	1	Palm	3	½	"	4	
30	17/11/39	2	Fingers	3	½	"	18	
25	13/12/39	1	Arm	3	6	"	25	
34	18/12/39	4	Hand, fingers	2, 3	1½	"	17	
—	10/1/40	2	Fingers	2	½	"	12	
46	6/2/40	4	"	2	6	"	4	
32	8/2/40	1	Hand	2	1	"	4	
37	24/2/40	1	Forehead	2	½	"	9	
28	7/3/40	1	Finger	3	½	"	11	
36	14/3/40	1	Hand	2	½	"	7	
38	15/3/40	1	Forearm	3	1½	"	23	
46	28/3/40	1	Finger	3	½	"	12	
36	2/4/40	1	"	3	1	"	18	
35	10/4/40	3	Fingers	3	1½	16	24	
34	25/4/40	1	Forehead	3	4½	Nil	60	
68	13/5/40	2	Forearm	3	1½	"	24	
47	15/5/40	1	Wrist	3	1	"	16	
42	23/5/40	2	Fingers	3	1	"	8	
29	2/6/40	1	Hand	3	4	"	35	
29	2/7/40	1	Finger	3	½	"	20	
36	4/8/40	3	Arm, forearm	3	32½	"	32	Skin eruption with acriflavine
45	21/11/40	1	Palm	2, 3	½	"	18	
38	25/11/40	1	Thumb	3	1½	"	27	
24	25/11/40	2	Wrist, hand	3	1½	"	39	Given light work
25	28/11/40	3	Wrist, fingers	2, 3	3	"	33	" "
37	29/11/40	1	Thumb	2	½	"	8	
—	4/12/40	3	Fingers	3	2	"	24	