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embolus on left side of brain; bilateral pulmonary basal œdema, bilateral pleural effusion, right greater than left; right fibrous pleuritis; ascites; passive congestion of liver; generalized œdema of skin; subacute nephritis, nephrotic syndrome; ? pulmonary infarction.

DR. SEGALL'S CLINICAL DIAGNOSIS

Rheumatic heart disease; mitral insufficiency; probable aortic stenosis; dilatation and hypertrophy of left auricle and left ventricle; thrombi in right and left auricle; congestive cardiac failure; pulmonary infarction due to either emboli or thrombosis of pulmonary arteries; bilateral pleural effusion; right ventricular insufficiency, general anasarca; cerebral embolus.

POSTMORTEM ANATOMICAL DIAGNOSIS

Rheumatic heart disease with mitral valvulitis and mitral insufficiency. Cardiac hypertrophy and dilatation. Patent ductus arteriosus. Mural thrombosis of pulmonary artery at the site of the ductus arteriosus. Mural thrombosis of left main and right lower lobe pulmonary arterial branches. Compression atelectasis of both lower lobes. Hydrothorax, bilateral. Ascites. Hydropericardium. Pitting œdema of legs and flanks. Œdema of leptomeninges. Chronic passive hyperæmia of viscera. Chronic bronchitis, severe. Pleural adhesions, bilateral.

ABSTRACTS OF AUTOPSY REPORT

The heart is markedly enlarged and globular in shape. Right auricular and ventricular chambers slightly enlarged. The pulmonary aorta is smooth and glistening except at the point where the ductus arteriosus leaves it; here an adherent pale red and grey mural thrombus is present. This thrombus extends into the left pulmonary artery but does not occlude it. The ductus is barely patent, the opening admits only a fine probe. The left auricle is considerably enlarged and is lined by grey, thickened, opaque, wrinkled endocardium, without thrombi. The mitral valve leaflets are thickened and slighly shortened. The chordæ tendinæ are thickened but not obviously shortened. The left ventricular cavity is somewhat enlarged and its walls are of average thickness. The aortic valve is normal.

DISCUSSION (by Dr. Segall)

The typical murmur of patent ductus arteriosus was not present in this case. There was the murmur of mitral insufficiency. It is very possible that there was a murmur of patent ductus arteriosus in this man a year before, but when we saw him in July, he already had a thrombus obliterating the patent ductus almost completely and, therefore, we did not hear the classical murmur. There was not much evidence to give us a clue to the existence of patent ductus arteriosus. It is unusual that he had these large mural thrombi and that they did not produce emboli. There was no pulmonary infarction. That is a very unusual pattern. We also have no evidence of a source of emboli to the brain and we were wrong in assuming that there was such an embolus. We must assume simply that he died of cerebral œdema, and that this œdema was related to congestive failure. The explanation should be found in the disturbances of metabolism to which malnutrition made some contribution.

Clinical and Laboratory Notes

PRE-ERYTHEMA BLOOD PRESSURE CHANGES FOLLOWING ULTRAVIOLET IRRADIATION*

C. A. FORSSANDER, M.R.C.S.(Eng.), L.R.C.P.(Lond.), *Montreal*

THE CLASSIC WORK on this subject was carried out by Johnson and his associates[1] in 1936. Using a carbon arc lamp for periods varying from 30 to 90 minutes, they found that the blood pressure was lowered in from five hours to five days after ultraviolet (U-VL) irradiation, returning to normal on about the sixth to ninth day. There was an average drop in systolic pressure of 6 mm. Hg, and 8 mm. Hg diastolic. Laurens[2] in a later paper records an average fall of 17 mm. systolic, with a range of 2-41 mm. and 2-20 mm. diastolic, and Graham[3] found a substantial change up to 7½ hours. These workers were interested in changes accompanying the erythematous reaction which follows U-VL irradiation by about two to eight hours.

The blood pressure changes recorded here are those occurring during the first hour after application of a mercury vapour† lamp. They were so immediate and so marked, even where special precautions were taken to ensure a basal state, that it appeared that an important physiological

*From the Department of Physical Medicine and Rehabilitation, Montreal General Hospital.
†Alpine: Hanovia.

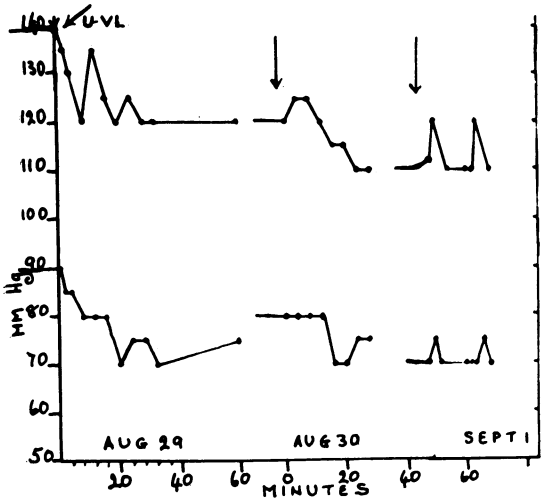

Fig. 1.—Case 1.

response was involved which was not directly related to peripheral vasodilatation. The possibility that the intermediate link is related to adrenal cortical secretion will be discussed in the light of these data.

RESULTS

CASE 1

A 54-year-old woman, suffering from cervical osteoarthritis and also hay fever, had received no previous ultraviolet radiation. Her resting blood pressure was 140/90 mm. After 24 hours in bed (up for toilet) she was wheeled to the treatment room and asked to lie down. Three consecutive blood pressure readings were taken at five-minute intervals and found to be steady, and the sphygmomanometer cuff was left in position; 24 sec. irradiation at a distance of 30 inches was then given in four stages covering the whole body. There was an interval of approximately one minute between each stage while the lamp was adjusted. The blood pressure was then taken immediately and then at two- or four-minute intervals.

The first graph shows that the systolic pressure, after several decreasing fluctuations, fell from 140 mm. to a steady level at 120 mm., where it stayed until the end of the hour during which it was observed. The diastolic also fell by 20 mm. by stages, and was beginning to rise when the observations ended. The only movement made by the patient was in turning on to her face for the third and fourth stages, and back again.

On the second day the same procedure was repeated, and the systolic pressure, which was steady at 120 mm. before radiation, rose temporarily to 125 mm. during the first eight minutes and then dropped steadily to 110 mm. The diastolic also dropped to the lowest level reached on the previous day and then rose to 75 mm. Hg.

Two days later the same procedure revealed a still lower starting point at 110/70 mm., presumably due to the previous irradiation, but no inclination to fall in the first 28 minutes after treatment, which consisted of 30 sec. radiation.

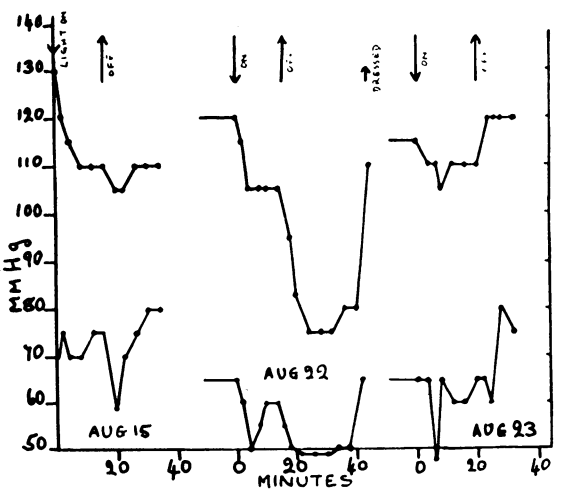

Fig. 2.—Case 2.

CASE 2

A 30-year-old male suffering from extensive psoriasis, but otherwise well and with no significant past history, had been attending for treatment for five days each week since August 1, and had therefore reached a higher dosage than Case 1. He was an outpatient. After sitting in the waiting room for 20-30 minutes he was asked to lie on a couch. Three consecutive blood pressure readings were 130/70 mm. at five-minute intervals. His previous irradiation had been three days earlier. As soon as the lamp was switched on, readings were taken at two- or four-minute intervals. The systolic pressure dropped rapidly to 110 mm., taking a further drop to 105 at the time that the light was switched off. On the other hand, the diastolic pressure rose. The dosage on this occasion was 19 minutes at a distance of 24 inches (60 cm.).

He had four further treatments without recordings. On August 22, since his skin reaction was rather severe, the dose was reduced, and a total of 16 min. 20 sec. at 24 inches was given. On this occasion the systolic and diastolic pressures started from a lower level, and quite an alarming drop occurred, without any subjective effects whatsoever. It may be significant that his pressure rose steeply when he stood up to put on his clothes.

The following day he was given a total of 14 min. radiation. The systolic pressure started a little lower again, but rose, together with the diastolic, quite sharply as the lamp was turned off. This cannot be explained and may be fortuitous.

The blood pressure appeared very labile, with a tendency to drop during the course of radiation, especially marked after a few days of particularly heavy dosage, and an inclination to rise sharply as radiation ceased. During the course of this the patient was quite relaxed, not interested in the procedure, and motionless on the bed. The diastolic pressure was particularly susceptible on this occasion, ranging from 48 to 80 mm. Hg in 22 minutes.

CASE 3

A healthy medical orderly, aged 22 years, with no significant history of illness, of very fair complexion, sensitive to sunlight, and under treatment for acne vulgaris, had received three very short treatments, of 8 sec., in June. In July he attended five times and was given 20 sec. In August he had been receiving 30 sec. five days a week, at a distance of 30 inches. His steady pressure of 125/85 mm. Hg rose after irradiation on August 15. After eight further treatments he was seen again, and again the systolic rose and fluctuated during complete rest, and simultaneous pulse readings (dotted line) showed a transient and significant increase in rate, with marked increase in force at the points marked with a + sign. The pulse changes were most marked on the following day (September 1), when for the first time his pressure, starting at the same basal level systolic

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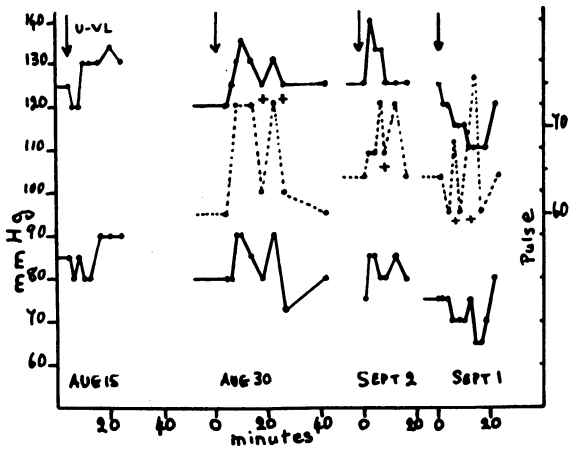

Fig. 3.—Case 3.

but a lower diastolic (presumably due to the erythema which had now developed), dropped to 110/65 mm. and then rose sharply. His pulse in the meantime became bounding and the rate had risen momentarily from 60 to 76 per minute. The following day, September 2, he once again showed a rise of pressure after treatment.

This case showed more clearly than the others an initial tendency for a rise, especially in the systolic pressure. Continuous intra-arterial pressure recordings might give additional data of value as it is not possible to observe more closely with the pressure cuff.

CASE 4

A man of 60 had suffered no serious complaints until August 29 when he developed severe low back pain while lifting a heavy weight. He was admitted to hospital and before receiving short-wave therapy and massage each day he was given U-VL radiation for experimental purposes. He was dealt with in the same manner as Case 1. He was of phlegmatic personality, and found to have a resting blood pressure of 125/65 mm. His first minimal dose of 20 sec. on September 2 produced an immediate drop of 15 mm. systolic and 5 mm. diastolic, with small pulse changes.

He was treated on September 3, 6 and 7 without recordings, and on September 8 his pressure was found to be 110/75 resting, dropping rapidly to 95/70 with slight excursions, after 120 sec. irradiation. His resting pulse rate had increased from 50 to 65, and fluctuated after irradiation quite widely between 56 and 68 per minute, with marked increase in volume at points marked with a + .

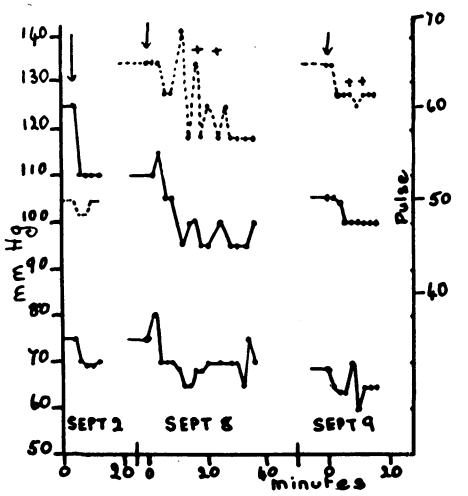

Fig. 4.—Case 4.

The following day (September 9) his resting pressure had dropped slightly to 105/68 and there was a slight further reduction to 100/65, with some uncertainty in the diastolic range. There was also a slight reduction in the pulse rate. The dosage on this occasion was 160 sec. at 30 inches.

DISCUSSION

The speed with which the blood pressure reacts to the stimulus of ultraviolet irradiation has not been stressed in the past, attention having been directed towards the changes occurring at the same time as the skin erythema, which appears several hours after treatment. In fact, since Finsen[4] in 1899 first reported that U-VL radiation causes a prolonged vasodilatation, the reduction in blood pressure has usually been considered to be a simple result of the peripheral vasodilatation.

Kovács[5] for example suggests that the blood pressure effects following the use of the carbon arc are not specific for U-VL, but perhaps due to luminous and infra-red components, and Ronge[6] feels that the primary result of erythema-active exposures is a vasodilatation followed by a diffusion of tissue fluids into the blood stream, resulting in dilution and increased blood volume. Krusen[7] lists cutaneous hyperæmia, decrease in blood viscosity, production of cutaneous depressor substances and creation of sympathetic hypotonia as possible causes of the blood pressure changes, and Lindhard[8] concluded that the effect of radiation is predominantly a cutaneous dilatation which, if not counteracted in some way, would increase the cardiac output, a measurement which Johnson *et al.*[1] found reached the highest value on the second or third day. Ellinger[9] suggested changes in thyroid activity as a factor, and Altschul[10] has recently remarked that although the most obvious explanation of blood pressure changes is dilatation of the peripheral vessels, the lowering of pressure lasts in many cases longer than the erythema. He has found a lowering of blood cholesterol level which, he suggests, sensitizes the vessel walls and thus permits the change.

When one reviews these many possible factors, it is not without hesitation that the possibility of adrenocortical activity is considered as one of the links in the chain of response to irradiation. Preliminary experiments seem to suggest that a reduction in circulating eosinophils follows U-VL irradiation. For instance, four hours after minimal exposure, Case 1 was found to have a reduction of 34% in the eosinophil count, and Case 4 a drop of 32%, after only 60 sec. exposure.

The relationship between increased activity of the adrenal cortex and stresses such as muscular exercise, trauma, cold, reduced atmos-

pheric pressure and certain toxic substances is well established. Selye[11] records that the transient leukopenia during the first few hours after U-VL irradiation, followed by a marked polymorphonuclear neutrophilia with lymphopenia reported by Wada,[12] is reminiscent of the eosinopenic reaction caused by other stressors. Dalton and Selye[13] and also Thorn *et al.*[14] regard eosinopenia as a sensitive and constant sign of hypophyseal activity in response to the action of ACTH on the adrenal cortex.

Consequently it is interesting to find that Graham[3] has noticed that the fall in blood pressure which follows carbon arc exposure is accentuated in adrenalectomized dogs, and that injection of desoxycorticosterone acetate or adrenal cortical extract abolishes the blood-pressure-lowering effect. This might suggest that an initial discharge of cortical hormones into the circulation after irradiation may be followed by an interval during which the blood pressure is lowered while the cortex recovers. Graham felt that the hypotension is due to vasodilatation, and that there is a humoral mechanism, probably adrenocortical. Blum[15] suggests that since the effect of histamine is enhanced by the removal of the adrenal cortex, and antagonized by adrenal cortical substances (assuming the local effects to be simply the "triple response" described by Lewis[16]) Graham's findings may indicate that blood pressure lowering is due to elaboration of histamine following irradiation. In this connection it may be noted that Menkin[17] has shown that injections of inflammatory exudate, or of leukotaxine, produce general capillary dilatation which is inhibited by injections of adrenal cortex. Partington,[18] however, has recently failed to demonstrate free histamine in the skin after irradiation, and points out that a flare is never seen around an area of skin reddened by U-VL, and Järvinen[19] has shown that cortisone raises the threshold required to produce reddening of the skin.

In the present work, only a minimal dose of U-VL could be used at the first application, which produced minimal physiological effects. Further, when the patient has had several treatments, and is able to take larger doses, the reactions to a single radiation are coloured by the prolonged effects of previous irradiation. For instance, it is known that blood pressure and cardiac output changes from a single dose,[1] may last a week or more, and additional irradiation must take that into account. This, at least in part, explains the pattern of the results. Another factor to consider is that varying degrees of exhaustion of the adrenal cortex may exist in a person subjected to intermittent radiation, and certainly will be present in anyone subjected to everyday stresses. Possible variations in extrinsic factors such as changes in position, posture, metabolism and emotional tension, were very carefully considered and eliminated as far as possible, and are not believed to influence the results significantly.

It is tempting to speculate. The concept of liberation of cortisone during the course of radiation helps to put this form of therapy on a rational basis, especially in relation to the rheumatic diseases, and incidentally might indicate why quiescent pulmonary tuberculous lesions tend to break down after irradiation, a danger also inherent in the administration of cortisone. We can at least say that studies of physiological response to radiation within the range 2,200 to 3,200 Angström units are incomplete, and appear to present a fruitful field for the investigator. Since the foregoing fluctuations appeared before the erythematous reaction, it seems reasonable to suggest that at least one other important factor besides peripheral vasodilatation is concerned in the blood pressure changes after U-VL irradiation.

SUMMARY

Blood pressure changes occurring before the development of the erythematous reaction resulting from ultraviolet radiation are described. A group of patients selected for their varied clinical background and dosage tolerance were closely observed over a period of up to one hour at two- to four-minute intervals. A mercury vapour lamp was used for periods of from one to 19 minutes. Pulse changes were also recorded. The results support the hypothesis that at least one other important factor besides an increase in peripheral vasodilatation is concerned in the blood pressure changes after U-VL irradiation, and activity of the adrenal cortex is considered.

I am indebted to Dr. Guy Fisk, Director of the Department of Physical Medicine and Rehabilitation, Montreal General Hospital, for his interest and support; also to Dr. Peter Morse for his assistance in recording the above observations, and Mrs. I. Pakalnans and Mrs. S. Camp from the School of Physiotherapy for their valuable co-operation.

REFERENCES

1. JOHNSON, J. R. *et al.*: *Am. J. Physiol.*, **114**: 594, 1936.
2. LAURENS, H.: *J. A. M. A.*, **111**: 2385, 1938.
3. GRAHAM, J. S.: *Am. J. Physiol.*, **139**: 604, 1943.
4. FINSEN, N. R.: *Presse méd.*, **2**: 17, 1898.
5. KOVÁCS, R.: Electrotherapy and light therapy, 6th ed. rev., Lea and Febiger, Philadelphia, 1949, p. 340.
6. RONGE, H. E.: *Acta physiol. scandinav.*, **15**: suppl. 49, 1948, p. 31.
7. KRUSEN, E. H.: Physical medicine, W. B. Saunders Company, Philadelphia, 1941.
8. LINDHARD, J.: *Skand. Arch. f. physiol.*, **30**: 73, 1913.
9. ELLINGER, F.: *Strahlentherapie*, **44**: 1, 1932.
10. ALTSCHUL, R.: *Arch. Phys. Med.*, **36**: 394, 1955.
11. SELYE, H.: Physiology and pathology of exposure to stress, Acta, Inc., Montreal, 1950, p. 409.
12. WADA, Y.: *Mitt a. d. med. Akad. zu Kioto*, **3**: 91, 1929.
13. DALTON, A. J. AND SELYE, H.: *Folia hæmat.*, **62**: 397, 1939.
14. THORN, G. W. *et al.*: *J. A. M. A.*, **137**: 1005, 1948.
15. BLUM, H. F.: *Physiol. Rev.*, **25**: 483, 1945.
16. LEWIS, T.: The bloodvessels of the human skin and their responses, 1st ed., Shaw and Sons, London, 1927, p. 117.
17. MENKIN, V.: *Proc. Soc. Exper. Biol. & Med.*, **51**: 39, 1942.
18. PARTINGTON, M. W.: *Clin. Sc.*, **13**: 425, 1954.
19. JÄRVINEN, K. A. J.: *Brit. M. J.*, **2**: 1377, 1951.