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APPENDIX

RESPIRATORY SYMPTOMS

Name..... X-ray No.....

	Yes	No
I. During the past 3 years, have you been ill with your chest? If yes:—		
Once only?		
More than once?		
Did you have increased cough?		
Did you have increased phlegm?		
II. (a) Apart from chest illnesses, do you usually have a cough? If yes:— Do you suffer from a persistently troublesome cough?		
(b) Apart from chest illnesses, do you usually bring up phlegm? If yes:— In the winter?		
Throughout the year?		
Is the phlegm usually yellow?		
If not: Did it become so during your illness?		
III. Do you ever get wheezing in your chest? If yes:—		
Slight-moderate?		
Severe?		
With chest illnesses?		
Does your chest ever feel tight? If yes:—		
Slight-moderate?		
Severe?		
With chest illnesses?		
IV. Have you ever had:—		
Year: Pneumonia?		
Pleurisy?		
Acute bronchitis?		
V. Do you consider that you suffer from:—		
Chronic bronchitis?		
Asthma?		
VI. (1) Is your breath as good as that of other people of your own age at work, on walking, hurrying, climbing stairs, or hills?		
(2) Are you able to walk with normal people of your own age on the level, but unable to keep up on hills or hurrying?		
(3) Are you unable to keep up with normal people walking on the level but able to walk a mile or more at your own speed?		
(4) Are you unable to walk more than 200 yards on the level without a pause for breath?		
(5) Are you breathless on talking, after undressing, or at rest?		
VII. Have you had to change your job on account of being too short of breath when at work? If yes: Year changed.....		
Job at which you failed.....		
VIII. Smoking:— Have you ever smoked?		
Now?		
Amount smoked now:— Estimated average during past 10 years if different:		
Cigarettes per day		
Oz. tobacco/week (hand-rolled)		
Oz. tobacco/week (pipe)		
Age at starting:..... Age at stopping:		
IX. Does observer consider subject to be bronchitic?		
X. Are you getting a pension for any chest disease?		
Have you ever applied for a pension?		

IRRADIATION-INDUCED MALIGNANT HYPERTENSION: CURED BY NEPHRECTOMY

BY

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The following case is considered worthy of record as, to the best of our knowledge, it is the first example demonstrating the possibility of saving life by timely nephrectomy where renal damage produced by irradiation has resulted in malignant hypertension.

Case History

A man aged 33 had his left testis removed for seminoma in 1941. Soon afterwards he complained of abdominal pain and distension and began to lose weight. A mass was found in the upper abdomen, but nothing was done until May, 1943, by which time the mass had become very large, extending well across the midline. He was given deep x-ray therapy by one of us (W. M. L.) in May and June, 1943, following which the mass disappeared, and he returned to normal health and full work. The total dosage to the left renal region was under 3,000 r. He remained well and at full work until July, 1954, when he was seen by one of us (S. O.), complaining of severe splitting vertical midline headache which had begun about a year previously and which was relieved by aspirin after about half an hour. Some six months ago a second type of headache had appeared, which was associated with a bounding pulse. Two weeks prior to the consultation he had found difficulty with his vision.

Because of various medical examinations for insurance purposes his blood pressure in 1950 was known to have been 150/90 mm. Hg; in 1952 it was 160/90 and in 1953 165/95.

There was a history of scarlet fever at the age of 18, but this was not complicated by nephritis, and there was no past history of pyelitis or urinary infection. There was no family history of hypertension or cardiovascular disease, and both his parents were alive, his father aged 76 and his mother 74.

On examination on July 22, 1954, the positive physical signs were that his apex beat was $4\frac{1}{2}$ in. (11.4 cm.) to the left of the midline in the fifth intercostal space, and a double thrust was visible and the cardiac impulse was forceful. A clear protodiastolic triple rhythm was audible, together with a faint systolic murmur at the apex. His aortic second sound was loud and musical. There were no aortic murmurs. His pulse was 78, of regular rhythm and large volume, but the vessel wall was not clinically thickened. His femoral, dorsalis pedis, and posterior tibial pulses were easily palpable. His blood pressure at rest was 215/130 mm. Hg.

On July 30 he was examined ophthalmologically by Mr. Ronald Crick, who reported some general retinal oedema with extreme attenuation of the arteries, which were hardly visible, and some dilatation of the veins. There was some deflection at the arterial crossings, with hard white exudate near the disk edges and more fluffy exudate farther out, with some flame-shaped haemorrhages. His disks showed a blurred margin, the right more than the left, with slight papilloedema. There was no nipping of the veins. The retinopathy was of Grade III-IV, and the whole process suggested a relatively acute and recent process.

There were no abnormal physical signs in the central nervous system, lungs, or elsewhere.

On clinical grounds, with knowledge of the gradual increase in blood pressure over the preceding three years, his

case was considered to be hypertension secondary to irradiation of the left kidney, rather than essential hypertension, and it was thought likely that he had suddenly entered a malignant phase over the previous six months.

In spite of complete bed rest and amylobarbitone sodium sedation, his triple rhythm persisted and the diastolic pressure did not at any time fall below 120 or the systolic below 180 mm. Hg.

Pre-operative Investigations

Teleradiograms of the chest in the antero-posterior and right and left anterior oblique views showed slight enlargement of the left ventricle.

The 12-lead electrocardiogram (July 22) showed severe ischaemia of the left ventricle as a result of hypertrophy of that chamber. The R wave was tall in leads V5, V6, VL, and standard lead I, and the S wave was deep in leads V1, V2, and V3. The T wave was inverted in leads V5, V6, VL, and standard leads I and II (see accompanying electrocardiograms).

An intravenous pyelogram showed delayed secretion of the left kidney with some deformity of the left lower calices. The right kidney was radiologically normal.

Chromocystoscopy by Mr. Yates-Bell showed slight delay on the left side, and micro-urea concentrations of ureteric urines showed slightly diminished concentration on the left side.

The blood urea was 44 mg. per 100 ml., and his urea clearance was 46% of the average standard normal. The urine showed a slight cloud of albumin with scanty red cells and pus cells and a few hyaline and granular casts. Urine culture was sterile. Haemoglobin was 108% and the red cells were normal.

Left nephrectomy was carried out by Mr. Yates-Bell on August 9. The perirenal fat was adherent and the ureter was found with difficulty among dense fibro-fatty tissue.

Pathological Report on Left Kidney (Professor H. A. Magnus).—The kidney weighed 84 g. The capsule stripped with some difficulty, revealing fine granulation of the kidney, especially on its greater curvature. On slicing, it was apparent that there was a very considerable reduction in the kidney substance with a corresponding increase in intrapelvic fat. At the lower pole there was one small cyst. The blood vessels were not unduly prominent and the renal pelvis appeared normal.

Sections showed numerous areas in which there was complete obliteration of glomeruli with marked arteriosclerotic changes in the associated blood vessels. These damaged areas of kidney tissue tended to have a linear distribution, but this was not a constant feature. In the areas of kidney tissue not involved the glomeruli were remarkably normal, but the arterioles and larger vessels still showed the changes of arteriolosclerosis. Towards the medulla the larger vessels showed pronounced medial hypertrophy and some fibrosis.

The histological picture suggested some process of long standing, and it may well have represented the end stages of damage from x-ray therapy. Professor Magnus stated that he had never seen a kidney in this condition, so that he was unable to make any comparison. He did not think the histological picture was that of malignant hypertension, and it was certainly not that of chronic nephritis. The vascular changes present in this kidney were not recent, and it was probable that they did not give a picture of what the vascular system was like as a whole. Had he not known the clinical history of the patient he would have suggested that the lesion represented the end-result of a chronic pyelonephritis.

Post-operative Progress

The blood pressure on the day after operation fell at one time to 130/80, but within a week it had reached 180/120 and a canter rhythm at the apex became again audible. At the time of his discharge from hospital on the 22nd day after his nephrectomy the blood pressure had reached

180/100. On that day Mr. Crick reported slight diminution of the oedema of both retinae; no haemorrhages were visible and the exudates were slightly less and the arterioles fuller than previously. The conclusion was that there was slight general improvement in the fundus picture. By September 8 the patient's blood pressure had reached 210/140.

On September 30 Mr. Crick reported that without doubt there had been a recession in the papilloedema and there was less attenuation of the retinal vessels, particularly noticeable in the right eye. In addition, some of the sharply defined glistening exudates which formerly made up

Electrocardiograms showing reversion to normal in less than a year after nephrectomy.

the pattern of the macular fan in the left eye had disappeared, so that there was now only one streak left in this formation, together with a few dots. No haemorrhages were visible.

By October 15 the blood pressure had fallen to 172/104 and the electrocardiogram showed slight improvement. The T wave, which previously had been inverted in lead VL and standard leads I and II, had become just upright. It was, however, still slightly inverted in leads V5 and V6.

A month later the visual acuity was 6/6 in each eye and there was a further slight improvement in the appearance of the fundi.

By December 22 he was quite well and working a full day, and had had no further headaches or nocturia, and he realized for the first time that he had been dyspnoeic prior to his operation. His blood pressure was 200/110, but there was no albuminuria. The electrocardiogram showed some further improvement in that the previously inverted T wave in lead V5 had now become upright, although inversion of the T wave in lead V6 persisted; the amplitude of the T wave in leads I and II had improved.

When next seen, on March 16, 1955, he was working hard and had no symptoms whatsoever; the blood pressure was 190/110 and the electrocardiogram remained essentially unchanged, with slight inversion of the T wave in lead V6 still present. His fundus picture showed still further improvement, the disks being flatter, the exudates fewer, and the vessels less attenuated. In view of the blood-pressure figure it was thought justified to try the effect of "serpasil" orally, 0.25 mg. three times a day. By April, 1955, the reserpine had reduced his blood pressure to the range of 150-160/92-110.

On June 22 the 12-lead electrocardiogram had become completely normal and the blood pressure was 162/94; he was now taking 0.5 mg. of reserpine thrice daily. Mr. Crick reported that his fundi had also now become completely normal.

When last seen on March 28, 1956, the patient had no symptoms whatsoever, was taking only reserpine, 0.25 mg. three times a day, the blood pressure was 152/92, and his 12-lead electrocardiogram was still normal in all leads.

Discussion

Radiation damage to the kidneys was first described by Ralston Paterson in 1952, and the material upon which his communication was based was analysed in detail by Kunkler, Farr, and Luxton in the same year. All the patients in this series—over 30—had been treated for testicular tumours with a radiation dose of from 2,000-3,000 r, distributed to both kidneys. The onset of renal failure was comparatively early, the interval after treatment averaging about eight months. In a number of cases the renal damage proved fatal. However, it was found that even in severe cases a considerable degree of recovery was possible after blood transfusion and prolonged rest.

In the case here reported the main incidence of the irradiation was on the left kidney, which received just under 3,000 r. The right kidney received a considerably lower dose, and part of this kidney must have sustained less than 2,000 r. Further, in considering the cause of the renal damage it must be taken into account that the kidney may well have been involved in the extensive growth which was present at the time of treatment. There can, however, be little doubt that radiations played a major part in producing the condition.

So far as we know, no case has previously been reported in which the picture of malignant hypertension has been produced by unilateral radiation damage, and we consider it important that this possibility should be recognized in view of the chance of cure offered by timely nephrectomy. Of all the malignant growths in the abdomen, seminoma perhaps offers the best prospect of cure by radiotherapy, and it is not unlikely that a proportion of the patients so cured suffer from malignant hypertension due to unilateral renal

damage. If this possibility is borne in mind at the follow-up of these patients lives may be saved.

Since Goldblatt's classical researches (Goldblatt *et al.*, 1934; Goldblatt, 1937, 1948) and those of Wilson and Byrom (1939) much interest has centred on the part played by human renal disease in causing hypertension, and in particular in the role of unilateral, or mainly unilateral, kidney disease. The exact cause of the high blood pressure in unilateral renal disease is still unknown, but it is probable that the diseased kidney secretes an excess of circulating pressor substance, and thus early removal of the kidney might be expected to reduce the elevated pressure.

The diseases which can give rise to unilateral or predominantly one-sided disease, with resultant hypertension, are numerous and may involve primarily the renal vessels or the parenchyma. Those conditions where nephrectomy has led to cure of the hypertension include chronic pyelonephritis, which is by far the commonest cause (Braasch, 1942), and such diseases as tuberculosis (Kennedy, Barker, and Walters, 1941), hydronephrosis, which usually results from an aberrant renal artery, neoplasm (Koons and Ruch, 1940), trauma (Farrell and Young, 1942), atherosclerosis of the renal artery (Leiper, 1944), infarction and undetermined cause (Perry, 1945).

In 1940 Schroeder and Fish laid down certain criteria for operation, among which was the absence of papilloedema and retinitis, but it is now realized that such malignant hypertension is by no means a contraindication to nephrectomy, as occasionally cure may result (Platt, 1941; Kennedy, Barker, and Walters, 1941; Powers and Murray, 1942; Leiper, 1944; Perry, 1945).

Recently Perera and Haelig (1952) have gone so far as to suggest that the type of hypertension induced by unilateral renal disease is in fact, malignant, being acute, severe, and rapidly progressive. Fourteen of their 16 adult cases showed retinopathy. They are of the opinion that as hypertensive vascular disease rarely, if ever, begins after the age of about 50 (Perera, 1948), the sudden appearance of a striking elevation in diastolic blood pressure in the older age groups, known previously to have been normotensive, should lead to a suspicion of unilateral renal disease.

Summary

An example is recorded of severe malignant hypertension induced by renal damage from irradiation that became normotensive after nephrectomy. Following nephrectomy, the blood pressure fell slightly over a period of seven months, and then responded at once, and satisfactorily, to moderate doses of reserpine orally. All symptoms disappeared after nephrectomy, and the continuous improvement of severe (Grade III-IV) retinopathy to complete normality within 10½ months of operation was paralleled by severe hypertensive electrocardiographic changes reverting completely to normal within the same period.

Attention is drawn to the possibility of saving life by timely nephrectomy where renal damage produced by irradiation has resulted in malignant hypertension.

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