requisite predisposing factors are present. Peery (1942) has recorded the finding of healed partial tears in the first part of the aorta. According to him, partial tears are usually encountered in the ascending portion of the arch, are usually transverse or oblique, and are rarely longitudinal. An essential predisposing factor, in Peery's opinion, is severe hypertension of long standing, and he is not certain that there need be any abnormality in the wall of the vessel. Microscopical sections from the aorta taken near the lesion, but not including it, usually do not show any recognizable abnormality. Arteriosclerosis is probably not a cause for this condition, since the tears seldom occur through an atheromatous plaque or ulcer. The precipitating factor in most cases is exertion, which, by raising the already elevated blood pressure, exceeds the pressure the aortic wall can stand, and rupture occurs.

Another predisposing condition is the presence of coarctation of the aorta, in which the vessel tears below the constriction, presumably owing to the increased pressure in that part of the artery (Moragues, Moore, and Rossen, 1942).

A few cases of partial rupture of the aorta have been recorded in which trauma was the immediate cause. In Heller's (1904) case the partial tear was due to a heavy burden falling on a man's chest. In the case reported by Oppenheim (1918) clinical manifestations followed a blow by a falling piece of granite. Nordlander (1925) and Oppenheim (1918) both referred to the occurrence of ruptured aorta in aviators falling from a high altitude.

The present case is unusual, if not unique, because of the method of production of the damage to the vessel. This man had a grossly hypertrophied heart, and, though his blood pressure was never recorded and there were no symptoms or other post-mortem changes to suggest it, he probably suffered from essential hypertension, though the fact that he had followed a strenuous occupation may have been partly responsible for the hypertrophy. There is no such lesion now recognized as idiopathic cardiac hypertrophy in an adult, and, in the opinion of Kugel and Stoloff (1933), it appears doubtful whether there is such a condition in infants and young children, as some workers maintain. The heart, as stated, weighed 793.5 g. According to Aschoff (1924) the normal heart weight in men is up to 355 g., while Parkinson (1936) quotes Evans to the effect that the upper limit is 390 g. By either of those standards this heart was grossly hypertrophied, and though many hearts weighing more have been reported (Strong and Munroe, 1940; Rosenow and Smith, 1939; and Royster, Lisa, and Carroll, 1941) some other factor in addition to essential hypertension has usually been present to account for the hypertrophy. The mechanism of production of the aortic lesions therefore seems to have been the increased pressure in that vessel. The sudden compression of the heart must have further raised the already high pressure in the left ventricle and aorta to such a degree that the vessel wall was incapable of withstanding it, and partial rupture ensued.

The clinical symptoms in cases of partial rupture of the aorta are always indefinite, and the literature does not seem to record a case in which this condition has been diagnosed ante mortem. According to Peery (1942), "the most common symptom is a choking sensation or a feeling of suffocation. Dyspnoea may come on suddenly and continue for some time. Pain is also a frequent symptom, and may be stabbing or tearing, although pain is less frequent and less severe when dissection supervenes immediately. Occasionally cough, haemoptysis, and fever are the presenting symptoms, and may be associated with pain of pleuritic type. The most important physical finding is undoubtedly the presence of heart murmurs. These may be either systolic or diastolic, and are usually best heard in the aortic area. The systolic murmur is as a rule harsh, and is probably due to vibration, in the blood current, of the abrupt shelf-like edge of the tear, or to eddying of blood over the small pouch between the lips of the tear. In a considerable proportion of cases, however, dissection of the aorta occurs days, weeks, or months later, with the usual manifestations of the condition. In other cases the clinical picture becomes one of aortic regurgitation with congestive heart failure." In the present case there was no immediate pain referable to the thorax, and two hours elapsed before pain started. Probably during that time dissection was not occurring

and the acute pain in the left side of the chest radiating through to the back became manifest when dissection through the media began to develop. Final rupture 26 hours after the original injury is in keeping with other cases reported and, as in a proportion of these, it occurred after some mild exertion—in this case sitting up in bed.

It is interesting to speculate what the outcome might have been if the patient had stopped work after the injury and gone to bed. Perhaps the intimal tears might have healed, as happened in the cases reported (Peery, 1942).

Many cases have been recorded in which hypertension has been associated with a unilateral renal lesion of some sort, and hydronephrosis is one of the conditions mentioned. Baggenstoss and Barker (1941) have reviewed the literature and reported a series of their own cases. Their series is short and, they admit, insufficient to draw statistical conclusions in the case of hydronephrosis, but they nevertheless tend to the opinion that this condition does not appear to influence the onset of hypertension. This aspect of the case is mentioned merely for the sake of completeness, in view of the work of Goldblatt (1940) and of Wilson and Byrom (1939) on the relationship between unilateral renal ischaemia and hypertension.

Summary

The clinical and pathological features of a case of rupture of the aorta due to a blow on the epigastrium are discussed.

Gross cardiac hypertrophy and essential hypertension are considered as factors in the mechanism of production of the aortic lesion.

The aetiology and symptomatology of partial rupture of the aorta are reviewed.

My thanks are due to Dr. James McCartan of Sheffield for particulars of the clinical history of the patient.

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A FATAL CASE OF PURPURA AFTER SULPHAPYRIDINE

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An opportunity recently occurred of making observations on a case of acute purpura occurring during the course of sulphapyridine therapy for pneumonia. As we have found records of only 18 cases in the literature, this seems to be one of the rarer complications of sulphonamide administration. For this reason we report the essential details of the case.

Case Report

On Oct. 12, 1943, a publican aged 52 became ill with a febrile condition diagnosed as pneumonia. Sulphapyridine was administered outside hospital, 30 g. being given in seven days. The immediate response was satisfactory, but five days after cessation of treatment a rise of temperature gave cause for anxiety. Recrudescence of pneumonia or empyema was considered. Sulphapyridine therapy was restarted, 4½ g. being given during the next five days. The malaise and pyrexia, however, persisted. It was noted that the temperature rose after each dose of sulphapyridine. On Oct. 28 there was slight

* Working on behalf of the Medical Research Council.

epistaxis. The patient was admitted to hospital on Oct. 30 for investigation.

Apart from trench fever in the last war the patient had enjoyed good health. He had not been subject to asthma, hay-fever, or urticaria; he had never taken sulphonamide drugs previously; and there was no personal or family history of a haemorrhagic diathesis. He was a heavy beer-drinker. An obese heavily-built man, he showed some difficulty in maintaining attention. Mucous membranes were pale. Temperature was 101.6°. The fundus oculi had some arterial thickening, but there were no haemorrhages. The nose was bleeding. There was much oral sepsis. B.P. 205/120. The chest revealed signs interpreted as those of a resolving right lower lobe pneumonia. Spleen and liver were not palpable. There was no enlargement of peripheral lymph glands.

By Oct. 31 the temperature was subsiding, and on Nov. 1 had become normal. B.P. was now 160/110. On this day an extensive purpuric eruption appeared on the palate, arms, and legs. Epistaxis persisted, and blood was oozing from the gums. Three times during the day he vomited coffee-ground material giving a positive benzidine reaction. The urine, normal in quantity, had become frankly blood-stained. The ankles presented pitting oedema.

On Nov. 2 his condition showed further deterioration. Purpura was even more gross, and blood was flowing freely from the nose and mouth. There were many submucous haemorrhages in the mouth, and in the tongue they were particularly well marked. Haematemesis and haematuria persisted. Sternal puncture was performed, and compatible blood was transfused through the site of puncture. As the procedure was started the patient complained of a bursting sensation in the head: 2½ hours later he was in coma. Respirations became laboured and gurgling, and blood-stained saliva was coming from his mouth. The fundus oculi, which earlier in the day had been clear, now showed numerous flame-shaped haemorrhages. There was a left hemiplegia, and plantar responses were bilaterally extensor. B.P. was 260/140. In a further 2½ hours coma had become profound. Fundal haemorrhages were more pronounced and blurring of the disk margins was observed. There was a flaccid paralysis of all the limbs. A finger-prick, made 2½ hours before, was still bleeding freely. Death rapidly supervened.

Investigations

X-ray chest, Nov. 1:—Left ventricle enlarged. Aorta unfolded. The appearances in the lung fields suggested bilateral recent resolving pneumonia. *Sputum* showed a scanty growth of *Strep. pneumoniae* and neisseriae. *Haematology*, Nov. 1:—Erythrocytes, 2,500,000 per c.mm.; Hb (Haden), 47% (7.33 g. per 100 c.cm.); C.I., 0.94; reticulocytes, less than 0.1%. Leucocytes, 10,000 per c.mm.: 3,200 lymphocytes, 6,000 neutrophil polymorphs, 500 eosinophils, and 300 monocytes. Platelets, 150,000 (direct method, using Lempert's modification of Kristenson's technique). Bleeding time (Duke's), 36½ min. (normal 2–5 min.); coagulation time (Lee and White), 27 min. (normal 5–8 min.); clot retraction, 1 hour (Macfarlane), 19% (normal 44–66%). Capillary resistance test by a positive-pressure method indicated very marked fragility. Smears of sternal marrow revealed no grossly abnormal features, except some preponderance of the myeloid elements. Megakaryocytes were present (0.4%), and these appeared normal. The leuco-erythrocytic ratio was 4.1. *Biochemistry* (7 hours ante mortem):—Plasma urea, 214 mg. per 100 c.cm. Plasma uric acid, 7.3 mg./100 c.cm. Plasma proteins, total 6.4 g./100 c.cm., of which 3.3 g. was albumin, 2.6 g. globulin, and 0.5 g. fibrinogen. Plasma bilirubin, less than 0.5 mg./100 c.cm. Plasma sulphapyridine: free 2.1 mg./100 c.cm.; total 4.44 mg./100 c.cm.

Urine Analysis.—On admission the urine was acid in reaction and contained albumin. The specific gravity was 1008. The centrifuged deposit showed only occasional leucocytes. Haematuria appeared on Nov. 1 and persisted. A sample passed 6 hours before death had a specific gravity of 1007, and albumin was present. There was no urobilinuria. Microscopy of the deposit revealed large numbers of red blood cells. Leucocytes were 6 per h.p. field, and there were very numerous coarsely granular casts.

Necropsy.—(34 hours after death; Dr. C. Keith Simpson.) The heart showed subpericardial, myocardial, and endocardial haemorrhages. Coarse purpuric haemorrhages were present throughout both lungs, causing extensive coarse nodular consolidation. No superimposed infection could be established. There was extensive purpura throughout the alimentary tract, mainly subperitoneal and with but little actual bleeding. The liver showed some purpura. Pulp haemorrhages were present in the spleen. Both kidneys were shot with innumerable purpuric haemorrhages resulting in virtual infarction. The renal pelves, ureters, and bladder contained no crystalline deposits and there was mild purpura only. The brain showed coarse purpuric haemorrhages into the cortex, into the white matter, including a vast area of confluent purpura in the right frontal lobe, and also into the ventricular system.

Histology (J. C. W.)—*Lungs*:—The essential lesion was a widespread haemorrhagic consolidation, mainly confluent. Intervening

areas were emphysematous, acutely oedematous, or collapsed. Infiltration of the alveoli by inflammatory cells was observed only at the periphery of the haemorrhagic areas. There was no unresolved pneumonia. The pulmonary capillaries were congested, particularly subpleurally. In some capillaries the endothelial lining cells were swollen. Myocardium revealed only scattered haemorrhages. Liver showed no gross pathological change. *Spleen*:—The splenic pulp contained scattered areas of haemorrhage, particularly in the subcapsular region. Moderate amounts of haemosiderin were demonstrated in the splenic pulp. *Kidneys*:—There were multiple haemorrhages. These were especially numerous in the subcapsular region, and formed wedge-shaped extensions into the deeper parts of the cortex. Focal areas of round-celled, mainly plasma cell, infiltration were scattered throughout. These bore no relation to any particular structure. The glomeruli were free from pathological change apart from slight thickening of the capsular basement membrane and occasional distension of the capsular space by red blood cells. There was considerable degenerative change in the epithelium of both convoluted tubules. A few of the collecting tubules contained acidophil hyaline material but no crystals. The interlobular arteries showed hyperplastic thickening and the afferent arterioles a slight degree of hyalinization. There was some increase in renal interstitial tissue, and large numbers of effete red cells were present. Little increase in collagen or reticulin could be demonstrated. Haemosiderin was practically absent.

Sections of femoral bone-marrow showed no architectural change.

Diagnosis

This patient's fatal illness could be attributed to the effects of sulphapyridine. The original lesion was a pneumonia, and the bleeding tendency did not become apparent until 16 days after the onset of this illness. At necropsy the pneumonia had resolved. A bleeding diathesis may be associated with nitrogen retention. In our case the plasma urea was 214 mg. per 100 c.cm. Though he was a hypertensive subject, the kidneys showed only moderate vascular changes. It would therefore appear more likely that the recent severe haemorrhagic changes in the kidney were responsible for impairment of function. In addition, the effects of gastro-intestinal haemorrhage would play a part in producing azotaemia (Black, 1942). The haemorrhagic state in our patient, therefore, was probably the cause rather than the result of the uraemia.

Discussion

The pathogenesis of sulphonamide purpura is a subject for conjecture. The drug is sometimes directly toxic to the bone-marrow. The structure of the sulphonamide drugs is similar to that of benzol derivatives having a known myelotoxic action. The occurrence of agranulocytosis and aplastic anaemia during sulphonamide medication is well known. In such cases thrombopenia associated with the aplastic anaemia (Meyer and Perlmuter, 1942) and the agranulocytosis (Dolgopel and Hobart, 1939) has been recorded. However, the red and white cell elements are usually well maintained in the peripheral blood in the acute purpuras associated with sulphonamide therapy, the former showing only a slight fall consequent upon haemorrhage, and the latter often being raised. Bone-marrow studies in our case revealed abundant megakaryocytes and increased cellularity, particularly of the myeloid elements. Similar findings have been reported (Markel and Rike, 1939; Russell and Page, 1940; Losada and Fernandez, 1942; Gorham *et al.*, 1943). More probably the purpura results from a generalized vascular defect.

In recent years the importance of the capillaries in the pathogenesis of purpura has been stressed (Mackay, 1931; Macfarlane, 1941; Scarborough, 1943). In all the 7 recorded cases of purpura following sulphonamide therapy in which the resistance of the capillaries was tested a marked fragility was noted. In 9 out of 12 cases the bleeding time was prolonged. In 4 of the reported cases, including our own, the platelet count, although low, had not been reduced to the level usually associated with bleeding in essential thrombocytopenic purpura. Scarborough in a recent personal communication mentioned a case of thrombocytopenic purpura following the local application of sulphathiazole ointment in which, after recovery from the acute phase, and when the platelet level was restored to normal, application of sulphonamide drugs to the skin led to a marked fall in capillary resistance in parts remote from the site of application. There was no significant change in the platelet count. The effect on the vessels may be due to hypersensitivity. If drugs are administered in two courses hypersensitive phenomena are more likely to occur. In our case

the drug was given for 7 days; then a 5-day interval was allowed to elapse before restarting it. It was only on the second occasion that the supposed intolerance became apparent. The only other instances of spaced dosage associated with purpura are recorded by Russell and Page (1940), Harries (1942), Werner (1942), Gorham *et al.* (1943), and Hurd and Jacox (1943). In 8 cases the administration was uninterrupted. Drug hypersensitivity may remain after recovery. Hurd and Jacox found that giving a small dose of sulphathiazole or sulphadiazine to their patient caused a marked fall in the platelet count with an increased bleeding time and a positive tourniquet test. Rosenfeld and Feldman (1942), however, were able to give a later course to their patient with no further purpura.

In the reported cases no member of the sulphonamide group of drugs seems exempt as a causative agent, and sulphanilamide, sulphapyridine, sulphathiazole, and sulphadiazine have all been held responsible.

The high mortality of this condition—8 out of 9 cases proved fatal—makes early recognition essential. The first clinical sign is nearly always epistaxis. If this or other spontaneous bleeding is discovered in a patient receiving sulphonamide drugs the administration should be stopped immediately and a bleeding time and capillary resistance test done. Adequate transfusion of fresh blood is probably the best line of treatment.

Summary

A fatal case of acute purpura occurring in the course of sulphapyridine therapy in pneumonia is recorded.

The pathogenesis of this condition is discussed. Vascular lesions as a basis for its causation are emphasized.

In view of its high mortality a watch for extraneous bleeding should be made in all cases receiving sulphonamide drugs.

We wish to express our thanks to Prof. J. H. Dible and Dr. J. McMichael for much helpful criticism. The necropsy findings are reported by kind permission of Dr. C. Keith Simpson.

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determined on a sample of blood from the ear, using the technique suggested by the Committee and a standardized Haldane haemoglobinometer.

Results

Most of the W.A.A.F. were between 18 and 25 years of age and all between 18 and 35. The distribution of the haemoglobin levels in the groups of W.A.A.F. examined is given in the accompanying Table according to length of service. Separate analysis of the results for the N.C.O.s and the W.A.A.F. personnel from the bomber station and training wing shows no significant difference, so these groups have been combined.

It is seen that all the groups who had been in the Service for more than six months had significantly higher haemoglobin levels than the group of W.A.A.F. just entering the Service, but that after six months to a year there is no further improvement. The coefficient of variation, however, becomes steadily smaller with longer service. The mean value for all those who had been in the Service for more than six months is 103.05, with standard deviation 9.12. The results have also been analysed according to trade. Some of the trades are represented by very few W.A.A.F., so that comparison has been possible only for a few. There is no significant difference between the results for cooks and butchers, motor transport drivers, clerks, aircraft hands (general duty), and telephone operators.* Analysis of the results according to age shows no significant differences in the age groups represented (18–35 years).

Table showing Distribution of Haemoglobin Levels of W.A.A.F. according to Length of Service

Hb %	On Entry	Length of Service				
		½–1 Yr.	1–2 Yrs.	2–3 Yrs.	More than 3 Yrs.	Total More than 6 Mths.
126–	..	1	2	—	—	3
121–	..	2	2	6	—	4
116–	..	6	9	6	1	18
111–	..	6	9	16	2	32
106–	..	41	8	18	22	53
101–	..	80	10	26	5	66
96–	..	118	4	25	32	64
91–	..	143	14	12	15	7
86–	..	87	2	3	7	0
81–	..	52	0	1	2	1
76–	..	10	1	0	1	2
71–	..	8	—	0	—	0
66–	..	3	—	0	—	0
61–	..	2	—	1	—	1
56–	..	0	—	—	—	—
51–	..	2	—	—	—	—
46–	..	0	—	—	—	—
41–	..	1	—	—	—	—
Total	..	559	48	108	127	24
Mean value %	..	94.84	102.46	104.10	102.71	101.62
Standard deviation	..	9.22	9.90	9.51	8.47	8.26
Coeff. of variation	..	9.72	9.66	9.14	8.25	8.13
						103.05
						9.12
						8.85

Forty of the W.A.A.F. from Group 1 were retested after ten months' service. The mean value of the haemoglobin levels of these girls on entry was 98.8 (standard deviation 8.32); after ten months the mean improvement was 4.25. This improvement is statistically significant (4.25 ± 1.70). The level reached is similar to that in the other groups with more than six months' service.

Discussion

Choice of Groups.—Almost all the girls in each group volunteered, so that there was practically no selection within the groups. The group of N.C.O.s were drawn from many stations to attend the course, and so constituted a fairly random sample of W.A.A.F. population so far as location is concerned. On the other hand, they were all training as N.C.O.s and were to that extent selected. They were presumably of more than average intelligence and their period of service was comparatively long; there was probably also some slight selection by trade. The group of W.A.A.F. from the bomber station and training wing, however, although selected as to location, were not selected by rank or trade. As the results for this group are not significantly different from those for the N.C.O.s,

* A smaller survey carried out on 82 W.A.A.F. aircraft fitters and 59 W.A.A.F. electricians showed the mean Hb of these to be 106.92 (standard deviation 10.2) and 106.87 (standard deviation 9.1) respectively. These figures are significantly higher than the mean for the general W.A.A.F. population after more than six months' service (difference 3.82 ± 0.91).

HAEMOGLOBIN LEVELS IN THE WOMEN'S AUXILIARY AIR FORCE

BY

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Between May, 1943, and April, 1944, a survey of haemoglobin levels among various groups of W.A.A.F. personnel was carried out. The main purpose of the survey was to determine whether the average haemoglobin levels showed any significant change during service in the W.A.A.F. In addition some of the results have been incorporated into the report of the nation-wide survey of haemoglobin levels initiated by the Haemoglobin Survey Committee of the Medical Research Council, whose report will shortly be published.

Plan of Experiment

The following groups were chosen: (1) W.A.A.F. personnel arriving to join the Service in May and June, 1943. (2) W.A.A.F. personnel attending an N.C.O.s' course in June, 1943. (3) W.A.A.F. personnel at a bomber station and a training wing in Sept., 1943. At each station all the personnel were asked to volunteer for the test, and, except at the training wing, almost all volunteered.

The girls completed a card giving information required by the Haemoglobin Survey Committee of the Medical Research Council (see Appendix). The haemoglobin level was then