throttle linkage and the car surged forward crushing his left leg between the bumper and garage wall. He sustained a compound comminuted fracture of the left tibia and fibula. Subsequently he made a satisfactory recovery.

Case 2.—A 25-year-old woman was admitted to the Royal National Orthopaedic Hospital in December 1967. She had been adjusting the accelerator cable of her Vauxhall Cresta motor car. As the engine speed was increased the car accelerated forward, running her over. The transmission had inadvertently been left in the drive position. She had a transverse fracture of the mid shaft of the right femur, traumatic separation of the symphysis pubis, fracture of the left superior pubic ramus, fracture of the left ischiopubic junction, undisplaced fracture of the medial wall of the right acetabulum, and numerous superficial lacerations. The lacerations were sutured, the fractured femur was treated with skeletal traction and the diastasis of the pubic symphysis was reduced with a pelvic sling. Next day she developed cerebropulmonary fat emboli, became unconscious, and required tracheostomy and intermittent positive pressure respiration for 10 days. Thereafter she made a satisfactory recovery and was discharged on 2 April 1968. She was subsequently readmitted for the excision of a bony spur which formed in the adductor region as a result of myositis ossificans and again for cosmetic reconstruction of her tracheostomy scar which had become keloid. When seen in August 1969, the right leg was 1·5 cm short and she had a slight ache in the right hip, which had a full range of movement. She could walk as far as she wished.

Case 3.—A man aged 44 was admitted to University College Hospital in July 1970. He had been leaning over the front of his taxi adjusting the accelerator linkage with the engine idling. The automatic transmission was in the drive position. As he increased the engine speed the taxi moved forward and crushed his left leg against the bumper of another taxi. He sustained a severe compound fracture dislocation of the left knee. After 10 weeks in hospital including open reduction of the fracture dislocation and skin grafting he continued mobilization as an outpatient. Five months after his injury he returned to driving an automatic taxi. One year after the injury his knee was pain-free but flexion was limited to 45° and there was slight instability of the medial ligament.

Case 4.—A 57-year-old man was admitted to the Royal National Orthopaedic Hospital in August 1971. The idling speed of his Austin 1300 car was too slow and he had been adjusting the slow running control of the carburettor. The automatic transmission was in the drive position. As he increased the idling speed the car surged forward crushing him against the garage wall. He sustained a posterior fracture dislocation of the right hip and superficial lacerations to both legs. The dislocation was reduced and after six weeks in traction he was mobilized. Subesquently he made satisfactory progress. One year after his injury he was walking with a slight limp. The hip was pain-free apart from an ache in the right buttock after walking one mile.

Discussion

Automatic transmission is becoming more popular each year and in 1971 it was fitted to 10% of motor cars produced by one large British manufacturer. Possibly as a result of rising charges, an increasing number of people are doing minor adjustments to their own cars. When adjusting the carburettor or throttle linkage of a car with manual transmission it is impossible for the car to be stationary with the engine idling unless the gear is in the neutral position. An automatic transmission, however, can be in the drive position with the engine ticking over and any tendency of the vehicle to creep forward counteracted by the application of the handbrake. If the engine speed is then increased by depressing the accelerator pedal in normal driving, or moving the throttle controls under the bonnet, the automatic transmission engages and the car surges forward easily overcoming the handbrake. Anyone leaning over the front of the car is either run down or crushed into whatever lies ahead. The consequences as described in the four case reports can be serious. Although this cause of severe injury is uncommon it should be preventable by an awareness of its possibility.

An automatic transmission should not be in the drive position while under-bonnet adjustments are being made with the engine running. It is suggested that an appropriate warning be included in the driver's handbook.

I wish to thank Mr. D. M. Brooks, Mr. E. O'G. Kirwan, Mr. E. L. Trickey, and Mr. J. N. Wilson for allowing me to report details of patients who were under their care.

MEDICAL MEMORANDA

Apparent Penicillin-induced Arrest of Mature Bone Marrow Elements

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We report here a case in which the patient developed pancytopenia after receiving large doses of penicillin. The pancytopenia seemed to be due to a blockade of the release of mature cells from the bone marrow—a process that might be termed "post-maturation arrest." This is the first time that such a hypothesis for the cause of the anaemia in these circumstances has been advanced.

Case Report

A 12-year-old boy was admitted to hospital in severe congestive heart failure due to rheumatic carditis. Cell-block preparations and smears of bone marrow showed hypercellularity with pronounced erythroid hyperplasia. The myeloid differential count was normal. One injection of benzathine penicillin, digoxin, mercurial diuretics, and iron were prescribed. He had not previously received penicillin. By the end of the third week there was no fever and the haemoglobin had risen to 11 g/100 ml.

On day 43 the patient developed fleeting hypertension, facial puffiness, microscopic haematuria, and mild proteinuria. Five days later he suddenly developed severe headache, meningismus, and a low-grade fever. On a provisional diagnosis of bacterial endocarditis, treatment with crystalline penicillin 20 megaunits/24 hr intravenously and streptomycin 600 mg/24 hr intramuscularly was begun. The meningeal signs and the fever disappeared in 48 hours and his general condition improved. After 10 days of penicillin therapy the Hb was 7·2 g/100 ml and the total white cells 8,200/mm³, with 5,000 neutrophils (61%) and 246 eosinophils (3%). Both direct and indirect Coombs tests were negative and remained so on four other occasions over the ensuing two weeks. On the 13th, 17th, and 22nd days of penicillin therapy (streptomycin was discontinued after 14 days) whole-blood transfusions of 250 ml were given. These raised the Hb to 11·8 g/100 ml. On the 18th day a nonpruritic papular rash appeared on the trunk. The white cell count was 3,300/mm³, with 660 neutrophils (20%) and no eosinophils. The total number of lymphocytes was relatively unchanged and there were no atypical forms. The platelet count was 80,000/mm³ and the reticulocytes 0·2%. The skin rash gradually became purpuric and there was one episode of epistaxis. Repeated tests for the presence of antipenicillin antibodies were negative. Immunoelectrophoresis showed, not unexpectedly, raised IgG.

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The penicillin was stopped after 23 days and a total dose of 460 megaunits. The next day the blood count showed white cells 2,300/mm³, with neutrophils 160 (7%) and platelets 40,000. Examination of bone marrow surprisingly showed hypercellularity with a myeloid-erythroid ratio of 3 : 1. The differential count (checked three different times on different slides) showed a pronounced and sudden shift towards mature cells in both the myeloid and erythroid series. There were more mature polymorphonuclear leucocytes and normoblasts than there were of their earlier forms. There were no cells of abnormal size and shape. The megakaryocytes and platelets were normal in number. Over the next two weeks the blood gradually returned to normal, and a reticulocytosis preceded a rise in haemoglobin to 13·4 g/100 ml.

Seventeen days after penicillin treatment had been stopped the patient was given a test dose of 1 megaunit of crystalline penicillin intravenously. No other new drug was given. Measures for resuscitation were available for immediate use. The only outward reaction was a mild, transient itching of the palms and soles. The most striking change in the peripheral blood count was a sharp drop in the neutrophil count from 6,500 to 840/m³ in 48 hours. In contrast, the total lymphocyte count dropped only slightly from 3,500 to 3,000/mm³. The counts of all other blood cells also fell slightly. Particularly interesting was a drop in reticulocyte count from 3·2 to 0·2%. Repeated direct and indirect Coombs tests were again negative. Three days after the test dose, when the neutrophil and reticulocyte counts were at their lowest, the bone marrow was hypercellular. Smears showed a myeloid-erythroid ratio of 4 : 1. Again the mature neutrophils and normoblasts outnumbered their earlier forms. The megakaryocytes appeared normal in number and shape. Within one week of the test injection white cells and platelets had returned to their previous levels and a reticulocytosis had begun. The patient was discharged on the 98th day after admission and has not been seen since.

Comment

In this case the relation between penicillin and the pancytopenia was proved by the challenge injection. The pathogenesis of the anaemia, however, was not the usual one of peripheral blood-cell destruction. The decrease in *all* the blood elements, including the reticulocytes (but not the lymphocytes), in the absence of detectable signs of haemolysis or leucocyte agglutination and lack of measurable levels of antipenicillin antibody point to involvement of the bone marrow. The paradox of a hypercellular bone marrow and peripheral blood pancytopenia can be explained in a number of ways.

Firstly, it might be due to a fortuitous sampling of an island of erythropoietic activity in an otherwise aplastic marrow (Movitt *et al.*, 1963). This is unlikely in our case in view of the rapid rise in the peripheral blood count after the discontinuance of therapy. A depleted marrow is unable to regenerate so promptly. Secondly, there might be intramedullary haemolysis with resultant pancytopenia, but a haemolytic process acting in the bone marrow and not in the peripheral circulation is difficult to envisage. Furthermore, the marrow showed no signs of a haemolysis and contained no abnormally shaped cells or macrocytes. Thirdly, a so-called maturation arrest of marrow elements is easily excluded in the present patient because mature cells rather than earlier forms predominated in the marrow, and the drop in the peripheral blood count was too rapid for such a process (Cronkite and Fliedner, 1964).

Finally, the paradox might be explained by impaired release of normal mature cells from the marrow. Katz *et al.* (1966) described a chemical mediator for the release of granulocytes from the marrow. King-Smith and Morley (1967) in their study of a release mechanism predicted that a mild degree of bone marrow failure would deplete the storage pool, thus removing the damping effect of the feed-back mechanism on the release of mature granulocytes and resulting in wide oscillations in the peripheral neutrophil count. This prediction was continued by Morley and Stohlman (1970), who produced cyclic neutropenia in dogs treated with small daily doses of cyclophosphamide. Morley and Stohlman (1969) also showed oscillations in the reticulocyte count of normal dogs, which they believed to be due to the same feed-back mechanisms.

We believe that the pancytopenia in the present patient was due to a penicillin-induced blockade of the release of mature cells of perhaps all three blood elements from the bone marrow. The rise in the reticulocyte count after stopping treatment and its abrupt fall after the test injection can also be taken to imply arrested release from the bone marrow. Finally, the surfeit of mature elements in the bone marrow suggests a blockade of their release. To propose an entirely new mechanism for anaemia on the basis of one case and without any of the elegant methodology needed for the study of the kinetics of erythropoiesis is perhaps too presumptuous. Nevertheless, our case calls attention to the existence of release factors and the part they might play in certain cases of bone marrow failure.

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Case of Cryptoccosis of Spine

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Clinically cryptococcal infection of the spine has been mistaken for tuberculosis (Koshi, 1961; Morris and Wolinsky, 1965). We report a case because of the rarity of spinal involvement and of the difficulty in diagnosis. Cryptococcosis produces a sarcoid reaction and when the organisms cannot be identified in tissue sections it may be mistaken for sarcoidosis.

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A 34-year-old Indian woman with mitral stenosis due to rheumatic heart disease had a first episode of pulmonary oedema during the last trimester of her fourth pregnancy. She was managed conservatively and had a normal delivery at term. Seven months later she had a mitral valvotomy, during which hard glands were found under the aortic arch. These were diagnosed histologically as sarcoidosis. She was discharged from hospital after 24 days, but six days later was readmitted with pain in the left side of the chest and dyspnoea. She was then found to have a gibbus over the fifth thoracic spinous process and was transferred to the University Hospital.

She was in pain, even lying down. Both submandibular and tonsillar glands were palpable and tender. She had coarse crepitations in the mid-zone of the left lung. Liver and spleen were not palpable. There was a tender gibbus over the fifth thoracic spinous process, but no neurological signs. Radiological examination showed a collapse of the body of the fifth thoracic vertebra with erosion of its left pedicle and a