lence. The suction-hole for this small vortex-venturi unit is placed just below the cell of the electric conductivity meter and helps scour this of small bubbles and also ensures a good flow of fluid through it.

Distribution of Dialysate

When the dialysate leaves the mixing-tank it passes into a delivery-tank which has an electric-heater element that may be used either to bring the dialysate up to temperature or for sterilizing the installation before use. The whole of the apparatus is made of materials which can stand chemical or heat sterilization, and it can be fitted with provision for either kind of sterilization. The components are all placed, either in the cabinet or in the rack for wall-mounting, in such a manner that each can be serviced in its place separately. The final mix is guarded by a second electric conductivity meter which can be set so that if its readings do not agree with the primary meter the alarm is set and the fluid is run direct to waste until the composition of the fluid returns to normal. A ring main can be provided to run round the ward if the unit is to be maintained permanently, or semi-permanently. Alternatively, multiple feeds can be plugged in if the mobile cabinet model is used.

The mobile cabinet model has had a clinical trial, and has proved to be reliable and satisfactory. The accompanying Table shows the constancy of the sodium concentration in the dialysing fluid. The electric conductivity meters have measuring-cells made of carbon-graphite composition and are robust, and have electrical constants of indefinite stability. They are unaffected by temperatures up to 80° C., by 2% formalin, or by 3% acetic acid. They require cleaning with detergent about once a month, and, if they are accidentally

damaged, cells with identical characteristics are available and may be kept as spares.

Sodium Concentrations of Dialysis Fluid

		Na mEq/l.	Dial Set to Give
2 Feb. 1966	3.30 p.m. (initial)	130	130 mEq/l.
	4.00 ..	130	
	4.30 p.m. ..	130	
	4.45 p.m. ..	131	
9 Feb. 1966	9.30 a.m. (initial)	130	130 mEq/l.
	10.30 a.m. ..	128	
	11.30 a.m. ..	130	
	12.30 p.m. ..	130	
	1.30 p.m. ..	128	
	2.30 p.m. ..	130	
	3.30 p.m. ..	130	
10 Feb. 1966	4.30 p.m. ..	128	130 mEq/l.
	9.30 a.m. ..	127	
	10.30 a.m. ..	129	
	11.30 a.m. ..	130	
	12.00 noon ..	128	
	12.20 p.m. ..	135	
	2.00 p.m. ..	136	
	3.00 p.m. ..	120	
	4.00 p.m. ..	120	130 mEq/l.

Summary

A machine for the automatic production of dialysing solution is described. The unit is based on a jet pump which adds a metered quantity of dialysing concentrate to tap-water. This unit has been in clinical use twice weekly for six months, and has been employed for over 150 dialyses in conjunction with the Longmore artificial kidney. It has been checked weekly for stability and found to be satisfactory.

The apparatus is manufactured by Medtec Tools Limited, 271 Argyle Avenue, Slough Trading Estate, Bucks, and we wish to thank Mr. Philip Allen, of Medtec, for the careful work which has gone into the manufacture of the prototypes. The cost of the unit varies with specification from £600 to £1,000.

Felty's Syndrome. Good Response to Adrenocorticosteroids: Possible Mechanism of the Anaemia

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The combination of chronic arthritis of the rheumatoid type, splenomegaly, anaemia, leucopenia, and often lymphadenopathy is known as Felty's syndrome (Felty, 1924).

The response of the blood abnormalities to adrenocorticosteroids is variable, but sustained improvement appears to be uncommon (de Gruchy and Langley, 1961). de Gruchy (1964) frankly states that they are ineffective. Splenectomy is often of considerable value (Hutt *et al.*, 1951; de Gruchy and Langley, 1961; Hume *et al.*, 1964) but tends to be hazardous, especially in the elderly patient.

The following case report illustrates a good response to adrenocorticosteroids, and studies of red-cell and plasma volumes and of red-cell survival with radioactive chromium (^{51}Cr) have served partially to elucidate the mechanisms by which the haematological improvement took place.

Methods

Occult blood tests: the amidopyrine method of Harrison (1957). Red-cell survival: method of Mollison and Veall

(1955) (^{51}Cr) after Pengelly and Wilkinson (1962). Mean red-cell life-span was calculated by method A (Mollison, 1956). Packed red-cell volumes: method of Wintrobe (1933). Red-cell volumes: method of Mollison and Veall (1955), blood samples being taken 25 and 30 minutes after injection of the ^{51}Cr -labelled red cells. Whole blood volume was calculated by assuming a whole body to peripheral haematocrit ratio of 0.91 (Gibson *et al.*, 1946; Chaplin *et al.*, 1953), the peripheral venous haematocrit having been corrected for trapped plasma by the method of Chaplin and Mollison (1952). The plasma volume was taken as the difference between whole blood and red-cell volume.

Case Report

A labourer aged 68 developed arthritis at the age of 47. Despite considerable deformity of his hands and feet he was able to work for 15 years until he was declared redundant. On 11 November 1964 he was admitted to the Grange Hospital, Weaverham, with bronchitis.

On examination a small pale man was seen with gross chronic rheumatoid changes in the hands, wrists, elbows, knees, ankles, and feet, and large nodules near the elbows. Scattered rhonchi were

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present in his chest. The spleen was enlarged to 5 in. (12.5 cm.) below the costal margin, and the liver was just palpable. Blood-pressure was 130/80. Urine contained an excess of urobilinogen. The rest of the examination was negative.

Investigations.—Haemoglobin 37% (100% = 14.6 g./100 ml.); colour index 1.09; white-cell count 600/c.mm. (polymorphs 11%, lymphocytes 61%, monocytes 21%, eosinophils 7%); platelets 60,000/c.mm.; E.S.R. (Wintrobe) 47 mm./hr. Test for L.E. cells negative. Rose-Waaler test negative. Stools negative for occult blood (×3). Sternal marrow showed active normoblastic marrow without any other abnormality. The direct Coombs test was weakly positive, but no abnormal antibodies were detected in the serum. Liver-function tests—thymol turbidity 5 units, zinc turbidity 9 units. Alkaline phosphatase 10 King-Armstrong units/100 ml. Serum bilirubin 1.0 mg./100 ml. Serum albumin 3.2 g./100 ml. Serum globulin 3.0 g./100 ml. Serum electrophoresis showed a decreased alpha-globulin. Barium-meal examination revealed evidence of an enlarged spleen but no other abnormality. Needle biopsy of liver showed only a few scattered groups of lymphocytes. X-ray picture of chest, I.V.P., blood urea, and mid-stream urine were normal. A red-cell survival test was carried out between 19 December 1964 and 9 January 1965. The mean red-cell lifespan was about 65 days. The haematocrit values and red-cell and plasma volumes are shown in the Table.

His chest infection responded to tetracycline. Prednisolone 10 mg. t.d.s. was started on 9 January 1965. There was an immediate improvement in his general state, the haemoglobin and white-cell count began to rise (see Chart), and on 28 January the haemoglobin was 72%, white-cell count 2,000/c.mm. (polymorphs 20%, lymphocytes 66%, monocytes 13%, eosinophils 1%). The platelet count was 210,000/c.mm. (The platelet count had started to rise before the steroid therapy was started). His spleen remained about the same size. He was putting on weight and was discharged from hospital very well on 11 February.

Prednisolone was reduced to 10 mg. twice daily on 15 March. On 10 May the spleen was impalpable. His haemoglobin was 80%, white cells 3,000/c.mm., and platelets 297,000/c.mm. The prednisolone dose was reduced to 5 mg. t.d.s. On 10 July the

prednisolone dose was reduced to 5 mg. b.d. and hydroxychloroquine sulphate (Plaquenil) 200 mg. t.d.s. was added.

On 14 January 1966 liver-function tests were completely normal, and E.S.R. (Wintrobe) was 30 mm./hr., and his blood picture was within normal limits. He was very well on 7 July 1966 and his blood picture was still normal (see Chart).

A second red-cell survival test was carried out between 20 October and 27 November 1965. The mean red-cell survival was again about 65 days. The haematocrit values and red-cell and plasma volumes are shown in the Table.

Discussion

In this patient studies of red-cell volume and survival indicated a mild haemolytic process, a normal red-cell volume, and a greatly increased plasma volume (see Table). Treatment with prednisolone resulted in a dramatic clinical improvement, with an increase in the haemoglobin and white cells to normal levels (see Chart) and considerable reduction in the size of the spleen. Further studies of red-cell volume indicated a reduction in the plasma volume from about 5.8 litres to about 4.3 litres (see Table).

Hume *et al.* (1964) thought the haematological improvement in their patients with Felty's syndrome after splenectomy to be due to the arrest of a haemolytic process, but they did not estimate plasma volumes. This has been done in other patients with anaemia and enlargement of the spleen whose plasma volumes were shown to be increased, notably by McFadzean *et al.* (1958) in patients with cryptogenetic splenomegaly; by Bowdler (1963) in a patient with Gaucher's disease whose plasma volume was reduced by splenectomy; and by myself in cases of malignant blood diseases with splenomegaly (Pengelly, 1965). Also Weinstein (1964) described five cases of "simple splenic hyperplasia" in which there was a marked reduction in the increased plasma volumes after splenectomy. Weinstein (1964) believed that the increased plasma volume was probably due to a change in the plasma oncotic pressure, and four out of his five patients showed reversed albumin/globulin ratios in the plasma before splenectomy. My patient also had slight changes in the plasma proteins, which became normal after corticosteroid therapy, but the significance of this change is uncertain.

Bowdler and Pranker (1965) suggest that an enlarged spleen can increase the size of the vascular compartment of the body, and that if the red-cell mass does not increase the plasma volume rises in compensation. For anaemia to occur this implies an impairment of bone-marrow function, for red-cell production can rise to six times the normal level in chronic anaemia (Giblett *et al.*, 1956). However, marrow impairment is quite probable in a chronic inflammatory disease such as rheumatoid arthritis (Weinstein, 1959).

In my patient it appears that the size of the spleen was reduced by the corticosteroid therapy, presumably as a part of a general reduction of reticuloendothelial hyperplasia, and that this has reduced the plasma volume in the same way as a splenectomy. This could be called a "medical splenectomy." On each occasion the red-cell volume was measured directly with ⁵¹Cr and the plasma volume was calculated on the assumption that the whole-body-haematocrit/venous-haematocrit ratio was 0.91 (Gibson *et al.*, 1946; Chaplin *et al.*, 1953). Verel

Haematocrit Values and Red-cell and Plasma Volumes

	Date	Weight	P.C.V. (%)	R.C.V.		Plasma V.		Whole Blood V.	
				Litre	ml./kg.	Litre	ml./kg.	Litre	ml./kg.
Before steroids	19/12/64	63 kg.	29.0	2.05	32.5	5.67	90.0	7.72	122.5
	9/1/65	" "	28.5	1.94	30.8	5.91	93.8	7.85	124.6
	Expected from weight (Dacie and Lewis, 1963)			1.76-2.21	28-35	2.52-3.15	40-50	3.97-5.67	65-85
	30/10/65	80 kg.	36.0	2.09	26.1	4.59	57.4	6.68	83.5
After steroids	27/11/65	" "	38.5	2.03	25.4	3.99	49.9	6.02	75.3
	Expected from weight (Dacie and Lewis, 1963)			2.24-2.80	28-35	3.20-4.00	40-50	5.44-7.20	65-8

(1954) and Fudenberg *et al.* (1961) have shown that in patients with very large spleens this ratio can well exceed unity. Ideally, direct plasma-volume estimations should have been made, but any gross error seems unlikely. If it is assumed that the true whole-blood volume in the first two tests was inaccurate and really as expected from his weight, then the body/venous haematocrit ratio would have to be between 1.2 and 1.8, which seem to be impossibly high figures. Fudenberg *et al.* (1961) noted a reduction in the whole-body/venous haematocrit ratio when there was oedema associated with adrenocorticosteroid therapy, but my patient never showed any clinical oedema, so the ratio is unlikely ever to have been below 0.91.

Summary

A case of Felty's syndrome is described in which the patient made a dramatic improvement with adrenocorticosteroid therapy. Red-cell volume and survival studies have shown that the improvement in the anaemia could be explained by a reduction in a grossly excessive plasma volume. It is suggested that inhibition of the reticuloendothelial hyperplasia by the steroid therapy has given the patient a "medical splenectomy," the benefits of this having been due to reduction in the size of the organ, with a reduction in the size of the body's vascular compartment, the same changes having sometimes been observed after splenectomy in patients who had had enlarged spleen.

My thanks are due to Dr. A. Fleming for asking me to take over and investigate the patient; to the Manchester Regional Hospital

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Preliminary Communications

Chromatography and Microbiological Assay of Vitamin B₁₂ in Smokers

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The hypothesis that one of the forms of vitamin B₁₂—hydroxocobalamin—is concerned in the detoxication of exogenous cyanide (Boxer and Rickards, 1952; Wokes and Picard, 1955; Wokes, 1958; Smith, 1961a, 1961b) has aroused much interest and speculation, and it has been suggested that inactivation of hydroxocobalamin by conversion to the cyano-form might be concerned in the pathogenesis of certain demyelinating disorders (Smith, 1961a). For some years it has been known that when serum B₁₂ is assayed microbiologically with *Lactobacillus leichmannii* the values obtained after extraction in the presence of added cyanide are usually much higher than those obtained when cyanide is absent (Boger *et al.*, 1955; Spray, 1955; Girdwood, 1960). The values obtained with added cyanide represent total serum B₁₂, while the low values obtained in the absence of added cyanide are associated with loss of the vitamin in the protein precipitate (Matthews, 1961, 1962).

Smith (1961a) stated that the difference between the values obtained with and without cyanide was "insignificant" in heavy pipe-smokers. He attributed this to the effects of the high cyanide content of tobacco smoke (Osborne *et al.*, 1956; Johnstone and Plimmer, 1959; Surgeon-General, 1964), and maintained that the value obtained without added cyanide represented serum cyanocobalamin, while the difference between this

and the value obtained with added cyanide represented serum hydroxocobalamin. Thus, according to Smith's hypothesis, the high proportion of serum B₁₂ extractable without cyanide in heavy smokers meant that most of their serum hydroxocobalamin (which he regarded as the physiologically active form) had been inactivated by conversion to cyanocobalamin.

Until recently there was no means of testing this hypothesis (Matthews, 1961, 1962; Basil *et al.*, 1965; Matthews *et al.*, 1965; Wilson and Matthews, 1966), since the forms of B₁₂ actually existing in the blood were unknown, but the development of suitable chromatographic and bioautographic techniques (Lindstrand and Ståhlberg, 1963; Lindstrand, 1964) has now made it possible to identify these components, which include methylcobalamin, hydroxocobalamin, and DNB coenzyme B₁₂. If the results of the "differential" microbiological assay (with and without added cyanide) do in fact reflect the proportions of B₁₂ components in the blood stream, this simple technique may be valuable, particularly in the investigation and diagnosis of conditions in which it is suspected that functional deficiency of B₁₂ may exist owing to excessive conversion to the cyano-form.

This communication reports an attempt to see whether increased amounts of cyanocobalamin could be detected in the plasma of smokers, and, if so, whether this could be related to the results of microbiological assay.

METHODS

Fifty-millilitre blood samples were taken from healthy volunteers, two non-smokers, and 10 moderate or heavy smokers.