could be the common factor to both systems. Modern advances have shown that the initial stage of blood coagulation involves the interaction of several factors, namely, antihæmophilic globulin, Christmas factor, platelets and factor V, to form active thromboplastin which in turn is capable of activating prothrombin to thrombin[5]. Factor VII, once thought to be essential for active thromboplastin formation, is now believed to be required only for the action of tissue thromboplastin on prothrombin[6].

If complement is related to any of these plasma or serum factors, it is not unreasonable to suppose that a congenital or acquired defect of a factor would be associated with a significant decrease or increase in the level of complement.

Serum from severely affected cases of hæmophilia, Christmas disease, factor V deficiency and cases treated with 'Dindevan' (factor VII deficient)[7] were examined for their content of complement as compared with normal blood examined under identical conditions.

In order to ensure accurate comparison the sera were derived from blood collected in siliconed glass without added anticoagulant. Platelet-rich plasma derived from these samples at 0° C. was allowed to clot at 37° C. in glass and the fibrin once formed removed. The resultant serum was tested for its titre of complement. While the platelet-rich samples undergo coagulation the platelets undergo a process of agglutination or lysis, at the same time releasing factors essential for hæmostasis and fibrin formation. As this process of cellular lysis might fix or destroy complement the titre of serum samples from platelet-free fractions obtained by differential centrifugation were compared with those of the sera from platelet-rich plasma (Table 1).

No significant difference in the level of complement was discovered between normal serum and serum derived from selected cases with specific coagulation defects. Similarly, there was no difference between sera from platelet-rich and platelet-free plasma.

It is unlikely, therefore, that antihæmophilic globulin, Christmas factor, factor V or VII are in any way related to complement or that complement is fixed during the interaction of these factors during blood coagulation. Neither is complement fixed by physiological agglutination or lysis of blood platelets.

Table 1. COMPLEMENT TITRES
1 volume serum + 1 volume 1·5 per cent sensitized sheep cell suspension

Serum	Complement titre (50 per cent) hæmolysis
Normal 1	1/16
Normal 2	1/24
Normal 3	1/16
Normal 4	1/32
Hæmophilia 1	1/16
Hæmophilia 2	1/16
Christmas disease 1	1/16
Christmas disease 2	1/24
'Dindevan' 1 } Factor VII	1/32
'Dindevan' 2 } deficiency	1/32
Factor V deficiency	1/32
Platelet-rich 1	1/24
Platelet-free 1	1/16
Platelet-rich 2	1/12
Platelet-free 2	1/16
Platelet-rich 3	1/24
Platelet-free 3	1/24
Platelet-rich 4	1/32
Platelet-free 4	1/32
Platelet-rich 5	1/32
Platelet-free 5	1/32

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Role of the Kidney in Erythropoiesis

RECENT observations in our laboratory indicate that the dynamic equilibrium of the erythron is controlled by the relationship of oxygen supply in the tissue to the demand for oxygen rather than by either alone. Conditions that reduce the demand for oxygen while the supply remains normal (acute starvation and the condition following hypophysectomy) and ones that increase the supply of oxygen while the demand remains normal (transfusion-induced polycythæmia and hyperoxia) all produce a profound decrease in erythropoiesis in rats. These animals give an exaggerated erythropoietic response to the injection of plasma rich in erythropoietin (anæmic plasma)[1].

Measures that increase the demand for oxygen while the supply remains normal (dinitrophenol or triiodothyronine) or that decrease the supply while the demand remains normal (bleeding or phenylhydrazine-induced hæmolysis) increase erythropoiesis in rats. Bleeding and the administration of phenylhydrazine constitute the standard procedures to obtain plasma with high erythropoietic activity.

Previous attempts to determine the site of formation of erythropoietin by surgical removal of organs[2] and by organ extracts have been unsuccessful[3]. With the sensitive assay methods available and the demonstration that a single dose of cobaltous chloride or an acute massive hæmorrhage greatly elevates the plasma erythropoietin-level of rats and rabbits within 10–12 hr.[4], we have been able to study this problem more thoroughly. We have reported that rats which have been subjected to hypophysectomy, thyroidectomy, splenectomy, adrenalectomy and gonadectomy retain the capacity to respond to repeated phlebotomy with an increase in the plasma content of erythropoietin which is comparable with that observed in similarly bled normal animals[3]. In addition, we have found that removal of seven-eighths of the liver, or removal of adrenals, spleen, pancreas, stomach, or intestines from the rat does not lessen the response to an injection of cobalt.

After bilateral nephrectomy, neither rats nor rabbits have the capacity to respond to a single dose of cobaltous chloride or a single massive hæmorrhage by an elevation of plasma erythropoietin. As shown in Table 1, the plasma obtained from the blood of

Table 1. Effect of Nephrectomy on Erythropoietin Production in Rats

Condition of donor	Stimulus	Assay of plasma (percentage of iron-59 incorporated into RBC)
Normal	Cobalt	9·8
Nephrectomized	Cobalt	2·4
Ureters ligated	Cobalt	5·5
Control	(Saline)	2·6
Normal (hæmatocrit 25)	Bleeding	15·4
Nephrectomized (hæmatocrit 33)	Bleeding	6·0
Adrenalectomized (hæmatocrit 35)	Bleeding	11·3
Control	(Saline)	6·9

In the first group the rats were injected with 76 μM cobalt chloride immediately after nephrectomy and 12 hr. after ureter ligation. The plasma was sampled 12 hr. after cobalt administration and assayed in starved rats. In the second group the rats were bled (6 ml.) immediately after operation, the plasma sampled 7 hr. later and then assayed in starved rats. A minimum of 5 rats was included in each group.

nephrectomized rats withdrawn 10–12 hr. after the injection of cobaltous chloride or after bleeding contains no erythropoietic activity as measured by the incorporation of iron-59 into the erythrocytes of starved[1] or hypophysectomized rats. Results with plasma from bled adrenalectomized rats are included to show that the difference in hæmatocrit is not responsible for the difference seen between unoperated and nephrectomized rats. Similar results were obtained when the erythropoietin titre was measured by the reticulocyte response in mice with transfusion-induced polycythæmia. The need for a control series of animals with the excretory function of the kidney removed, while the possible endocrine function has not been disturbed, is obvious, but at this stage of our work such an experimental preparation has not been achieved. As an approach to such a preparation we have, however, studied rats and rabbits after tying off both ureters.

In order to attain a uræmia at least equal to that which occurs 12 hr. after nephrectomy, we have waited 12 hr. after tying the ureters before giving cobaltous chloride or bleeding the animal, then 12 hr. later (24 hr. after the operation), we collected the blood and assayed the plasma for erythropoietic activity. The plasma erythropoietin level as measured by the uptake of iron-59 (or the reticulocyte response) was only slightly less than that observed in similar assay of anæmic plasma (Table 1).

The blood urea nitrogen of nephrectomized rats reaches a value of 70–90 mgm. per cent by 12 hr. as compared with control values of 21–22. Twenty-four hours after tying off the ureters, the blood urea nitrogen in rats reached values between 125 and 150.

It is possible that the toxic reaction resulting from nephrectomy is sufficiently different from that which results from tying off the ureters to suppress erythropoietin at some site, other than the kidney, in the nephrectomized animals but not in animals that have both ureters tied. Another possibility, not yet tested experimentally, is that erythropoietin is produced as an inactive precursor somewhere other than in the kidney and must be activated by the kidney before its presence can be detected by our assay method. Since, however, the assay is done in an animal with intact kidneys, this possibility seems unlikely. There still remains the alternative explanation that erythropoietin is produced as an inactive precursor by the kidney and is activated by some other tissue. This, however, would not alter our conclusions.

These observations indicate that the rate of erythropoiesis, or, taken as a whole, the dynamic equilibrium of the erythron, is controlled by the amount of circulating erythropoietin, and that its production in the kidney is determined by the oxygen supply–demand relationship of the body. We suggest that the metabolic pattern of the normal animal is determined by many factors, but chiefly perhaps by the endocrine glands. Once the metabolic level is established, the dynamic equilibrium of the erythron is automatic, but it will respond to the various stresses of a normal or abnormal physiological nature that affect the oxygen demand–supply relationship or that interfere with the production or utilization of erythropoietin.

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Benthic Fauna of the Continental Edge off Accra, Ghana

The continental edge off Accra occurs at a depth of about 100 m., about 16 miles offshore. The bottom at this depth consists of outcrops of sandy marine limestone with areas of coarse, calcareous muddy sand with much dead polyzoa, shell and coral material.

This area, between 70 and 100 m., is of interest not only because much of the fauna found has never before been recorded for tropical West Africa but also because this fauna appears to be very exactly related to that found at similar depths in the western Mediterranean in those bottoms which have been termed the '*fonds coralligènes*'. The rock epifauna is dominated by massive colonies of the coral *Dendrophyllia ramea* (L.) to which are fixed large numbers of *Ostrea cochlear* Poli and *Balanus tulipiformis* Darwin. The echinoderm *Astrospartus mediterraneus* (Risso) is common, clinging to a yellow *Gorgonia* sp. to which also large numbers of the lamellibranch *Avicula hirundo* (L.) are attached. The only West African endemic found in quantity is *Antedon hupferi* Hartlaub. This assemblage of fauna is an exact repetition of that reported by Gruvel[1] off Agadir in Morocco at depths of 75–120 m. The Agadir fauna is typically Mediterranean–Atlantic and similar assemblages have been recorded from several points in the western Mediterranean[2]. The fauna of the muddy sand off Accra at similar depths is equally Mediterranean in its affinities. The dominant species is the solitary coral *Caryophyllia clavus* Scacchi, but colonies of *Cladocora patriarcha* Pourtalès are not uncommon. This last species has been recorded from two localities in the Mediterranean but was first described from off the Brazilian coast and is recorded