The increased excretion of D-glucaric acid during human pregnancy[2] was reflected by a rise in the liver dehydrogenase activity of pregnant mice, also shown in Table 1. This change was more marked when comparing total liver enzyme activity, due to the increased organ weight of the pregnant animals. A decrease in the enzyme activity of uninvolved liver tissue occurred in mice bearing experimental tumours produced by the subcutaneous or intraperitoneal injection of tumour-cell suspensions (Table 2); autopsy specimens of histologically tumour-free liver from human subjects with cancer have also shown considerably reduced dehydrogenase activity.

Speculation on the significance of these changes must await investigation of the possible physiological action of the D-glucarate produced, for example, as a potential inhibitor of endogenous β-glucuronide hydrolysis.

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Enzymatic Cyclization of L-Glutamine and L-Glutaminyl Peptides

THE following observations suggest that papaya latex contains an enzyme which catalyses the cyclization of L-glutamine and of L-glutaminyl peptides.

When commercial crude papain or dried papaya latex was added to a solution of L-glutamine and the *p*H adjusted to 7–12, free ammonia was formed at the expense of amide ammonia. At the optimal *p*H of 10, 1 mg of the soluble fraction of crude papain (Merck) caused the liberation of 0·057 μmole ammonia from 0·025 M L-glutamine solution per minute at 30° C. Paper chromatography showed that the glutamine was simultaneously converted to a compound which did not stain with ninhydrin, but which stained with starch-iodide following chlorination[1], and which had the same R_F in *n*-butanol/acetic acid/water (4 : 1 : 1) as pyrrolidone carboxylic acid.

These changes were not observed with D-glutamine, or with crude papain solution which had been heated at 90° C for 20 min. They were not substantially affected by dialysing the papain or by pretreating it with iodoacetate (0·01 M) or ethylenediamine tetraacetic acid (0·01 M). Pure papain and chymopapain were inactive. Unlike the non-enzymatic cyclization of glutamine[2,3], the foregoing reaction was not accelerated by phosphate or bicarbonate.

Glutamine derivatives such as L-glutaminyl–L-leucine and L-glutaminyl–L-asparagine were de-amidated and converted to ninhydrin-negative compounds by crude papain considerably more rapidly and at a lower *p*H than L-glutamine.

Damodaran and Ananta-Narayanan[4] examined the formation of ammonia during enzymatic proteolysis and concluded, *inter alia*, that crude papain contains a de-amidase. The possibility that this de-amidase is identical with the foregoing enzyme is at present being investigated.

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Iron Metabolism in Avian Erythroblastosis

EARLIER work[1,2] has indicated a disturbance in iron metabolism in avian erythroblastosis, a virus disease of chickens in which there is an erythroblastic hyperplasia of the bone marrow with the entry of primitive red cells into the circulating blood. In normal birds injected intravenously with iron-59, the radioisotope disappears from the plasma and reappears in 24–48 h. In birds with erythroblastosis the activity reappears more quickly[1], autoradiographic investigations in blood smears suggesting that most of the activity is associated with the primitive cells[2].

Combined electrophoretic and autoradiographic studies, made on a limited scale, have shown that most of the radioactive iron in the cellular elements of leukæmic blood is not in the form of hæmoglobin. Similar *in vitro* studies were made. Blood samples from five normal and eight leukæmic birds were incubated with iron-59 and aliquots were removed at 6 and 24 h. The samples were separated into plasma and red cells, and hæmolysates were made of the latter. Both plasma and hæmolysates were subjected to electrophoresis and autoradiography. As incubation of the normal blood proceeded, radioactivity in the plasma β- and γ-globulin bands declined parallel with its appearance in the hæmoglobin bands. In two of the five normal blood hæmolysates, a small amount of activity was present in a component other than hæmoglobin. This component migrated with about half the speed of the slowest hæmoglobins, comparable with the speed of fowl 'ferritin'[3]. Autoradiographs of electropherograms prepared in the same way from the eight *in vitro* incubated leukæmic bloods showed marked radioactivity in a position corresponding to this slow band with only slight activity in the hæmoglobin region.

Two alternative explanations can be offered: either 'blocking' of iron occurs at an early stage in the synthesis of hæmoglobin, or diversion of iron occurs to sites other than hæmoglobin. In the former the intermediate would accumulate in the primitive cells, with elevation of non-hæm iron; in the latter such an increase would not occur. It was thought that determination of non-hæm iron in the liver and whole blood would help point to the correct alternative. Kennedy's thiocyanate method for total iron[4] was used with normal and affected livers; a micro-modification was used with whole blood[5]. Non-hæm iron was determined by these methods after its extraction by pyrophosphate[6]. All figures obtained are based on the average of duplicates. Adult birds (6 normal and 10 leukæmic) were used for the liver determinations and five-week-old chicks (17 normal and 32 leukæmic) for the blood determinations. The non-hæm iron was markedly elevated in the liver but not in the whole blood (Table 1). Blood smears stained for iron by Perl's method also failed to show evidence of free iron in the mature or primitive cells. The absence of a major elevation of non-hæm iron in the blood could point to a cycling of iron through the cells without it reaching hæmoglobin and, instead, reaching a non-hæm iron pool in the liver (and possibly the spleen[1]). The non-hæm iron in the liver is bound to a protein with some of the properties of a ferritin. The protein is heat resistant, contains non-hæm iron and is precipitable with 35 per cent ammonium sulphate and 4 per cent cadmium sulphate[7].

These observations raise many questions, which include the following: Is the non-hæm iron complex appearing in the *in vitro* cultivated blood 'ferritin'? Is the disturbance

Table 1. TOTAL AND NON-HEM IRON IN THE LIVER AND BLOOD OF NORMAL BIRDS AND BIRDS WITH ERYTHROBLASTOSIS

	Normal	Erythroblastosis
Total iron		
Liver (mg/g tissue)	0·87 ± 0·07	2·98 ± 0·44
Blood (mg/100 ml.)	28·37 ± 0·66	23·44 ± 0·70
Non-hæm iron		
Liver (mg/g tissue)	0·58 ± 0·05	2·79 ± 0·49
Blood (mg/100 ml.)	1·85 ± 0·20	2·14 ± 0·20