$\Delta G^{\neq}$ and $\Delta H^{\neq}$ corresponds to quanta with wavelength of ≈ 2 μm. This value lies just in the domain in which the electromagnetic emission of the active nerves was detected[19].

The fact that $\Delta S^{\neq}$ always has large negative values shows that the active state of the membrane is a more ordered one. It appears that, during the excitation, the entropy of the membrane firstly decreases, after which it increases, while the entropy of the axoplasma and the interstitial fluid only increases due to ionic fluxes[20]. These opposite entropy changes offer a basis for the understanding of the biphasic form of the initial heat production associated with a nerve impulse[17,21]. All the attempts to explain this fact solely on the basis of ionic fluxes failed. The optical changes associated with nerve impulse propagation[3-5] indicate the occurence of structural changes in the membrane and even seem to indicate a decrease in entropy. The calculations presented here clearly show such a decrease, and we can get an idea of the magnitude of structural changes, remembering that the formation of a hydrogen bond is associated with $\Delta H = 4.5$ kcal/mol and $\Delta S = -12$ cal/mol °K. Accordingly, the structural changes occuring in each membrane subunit are energetically equivalent with the formation of up to 5 hydrogen bonds.

Résumé. La théorie du complexe d'activé est appliquée à la description de la propagation de l'influx nerveux. On déduit les formules donnant tous les paramètres d'activation de ce processus et on les calcule pour différent types de fibres nerveuses. L'entropie d'activation est grande et négative, ce qui prouve que la membrane excitable est dans un état plus ordonné pendant l'excitation. L'énergie libre d'activation est presque la mème pour toutes les fibres nerveuses. Elle peut donc être considérée comme un paramètre fondamental de la conduction nerveuse.

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Embryonic Megaloblastosis

A consistent feature of embryonic development is the change from a megaloblastic haemopoietic cell line to one which is normoblastic. This has been well documented in the chick embryo[1], but few studies – other than morphological ones – have been undertaken to determine the cause. The question was asked whether megaloblastosis in the embryo could be related to the metabolic defect occurring in orotic aciduria, where there is very little activity of the enzymes, orotidylate pyrophosphorylase and decarboxylase, and resultant megaloblastosis[2]. The developing chick embryo was used as a model.

Fertilized fowl eggs were incubated at 37 °C for time intervals up to 4 days. Blastoderms dissected from the eggs were classified according to the stages defined by HAMBURGER and HAMILTON[3]. Embryonic or blood island tissue was homogenized for estimation of combined orotidylate pyrophosphorylase and decarboxylase levels by the release of radioactive CO_2 from orotic acid, labelled in the carboxyl group[4].

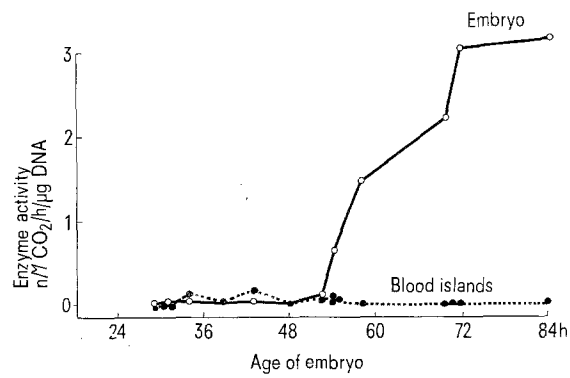

Fig. 1. Combined orotidylate pyrophosphorylase and decarboxylase activity in chick embryonic (open circles) and blood island (closed circles) tissues, at different stages of development.

The results of estimation of enzymatic activity in embryonic or blood island tissue at different stages of development from 24 to 84 h are shown in Figure 1. In the embryo, enzymatic activity was barely detectable by this method until 55 h, when there was a striking increase. In contrast, in the blood islands, activity remained at a low level until 55 h, but the subsequent rise in activity was masked by a parallel rise in DNA content – that is, relative activity in the blood islands did not alter with age. Similar trends were obtained when enzymatic activity was compared with protein.

The relative lack of this essential step in de novo pyrimidine biosynthesis during the early stages of chick embryogenesis is interesting in view of the active DNA synthesis occurring at this time. DNA synthesis may depend on other sources, such as the salvage pathway (uridine kinase). In view of these findings, orotidylate pyrophosphorylase and decarboxylase activity was compared with that of a control enzyme in the purine pathway, hypoxanthine-guanine phosphoribosyl transferase (HGPRTase), which converts hypoxanthine to inosine monophosphate. HGPRTase is also a salvage enzyme. Figure 2 shows that this enzyme was present from the beginning, and its activity was gradually reduced in both embryonic and blood island tissue at all stages of development.

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Until 48 h, the predominant cell formed is the megaloblast. Although further production of megaloblastic cells gradually ceases after 48 h, existing cells continue to mature and the low enzymatic activity sustained in the blood islands coincided with the continuing presence of megaloblasts. There appeared to be a correlation between the increase in enzymatic activity at 55 h and the appearance of immature normoblasts in the circulation. The dramatic change in the embryo at 55 h may be the result of induction of the de novo pathway for cellular development, and perhaps normoblastic maturation. Embryonic megaloblastosis may, therefore, be related to a metabolic defect in the conversion of orotic acid to uridine monophosphate[5].

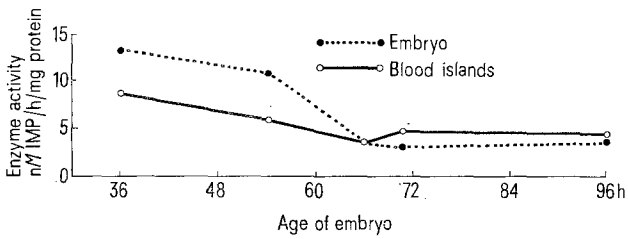

Fig. 2. Hypoxanthine-guanine phosphoribosyl transferase activity in chick embryonic (closed circles) and blood island (open circles) tissues, at different stages of development.

Résumé. La mégaloblastose embryonnaire peut apparaître à la suite d'un défaut métabolique dans la biosynthèse de novo des pyrimidines dans la conversion d'acide orotique à l'uridine 5-phosphate.

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[5] This investigation was supported by a grant from The National Health and Medical Research Council of Australia.

Effect of Spironolactone and Phenobarbital on the Plasma Fibrinogen in Rats

For more than 50 years evidence has been accumulating that fibrinogen is formed in the liver. The microsomes are considered to be the site of the synthesis within the cells while the fibrinogen in the soluble fraction is in storage[1].

Recently, it has been shown that spironolactone (SNL) – formerly known as an antialdosterone steroid without any other hormonal activity – greatly increases the de novo synthesis of several microsomal enzymes, protein, phospholipid, RNA and hemoprotein content in the liver[2,3] and consequently induces resistance in the body against many structurally unrelated exogenous and endogenous toxic substances[4]. Morphologically a marked proliferation of the smooth surfaced endoplasmic reticulum was observed[5].

In order to elucidate further interrelationships we studied the effect of SNL – in comparison with that of phenobarbital – on the synthesis of fibrinogen. That is the reason why the plasma fibrinogen level was measured, since this represents approximately 75% of the total body fibrinogen.

In another series of experiments, C^{14}-labeled amino acids were given and the radioactivity of fibrinogen was determined, in order to exclude the possibility that the increased fibrinogen level was due to a release of fibrinogen stored in compartments which were not in transfer-equilibrium.

Materials and methods. 200 female rats of Wistar strain with a mean body weight of 100 g were divided into 3 groups and treated with SNL or phenobarbital in a dose of 20μM/100 g body wt. twice daily perorally for 3 consecutive days. The first group treated with H_2O served as a control.

For determinations blood was taken on the 4th day after overnight fasting, and liver was quickly removed and weighed. Plasma fibrinogen was determined according to GRANNIS[6] as a clottable protein by adding thrombin in the presence of soybean trypsin inhibitor and ε-amino-

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Effect of spironolactone and phenobarbital on liver weight, plasma fibrinogen level and the incorporation of C^{14} amino acids into fibrinogen

Group	Treatment	Liver weight (g) means ± S.E.	Fibrinogen in plasma (mg/ml)	Radioactivity of fibrin at the time of maximum incorporation (dpm/mg fibrinogen)
1	Control	3.4 ± 0.15	2.6 ± 0.16	6 h after giving C^{14} amino acids 410
2	Spironolactone	4.0 ± 0.08[a]	3.4 ± 0.21[a]	3 h after giving C^{14} amino acids 980
3	Phenobarbital	4.5 ± 0.14[a]	3.9 ± 0.42[a]	33 h after giving C^{14} amino acids 1170

[a] Significantly different from group 1.