of living tubercle bacilli in the lungs of the cortisone rabbits, their dissemination to the draining tracheobronchial lymph nodes was very much less than in the control animals.

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The Adaptive Increase of the Tryptophan Peroxidase-Oxidase System of Liver

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The activity of the recently discovered system in liver converting tryptophan to kynurenine (*1*) increases following the administration of tryptophan and certain other substances to an animal. This increase is referable to the tryptophan peroxidase-oxidase system, which is an example of a physiological "coupled oxidation" (*2*): a peroxidase reaction specific for L-tryptophan followed by a second oxidation to formyl-kynurenine, using oxygen and producing hydrogen peroxide for the first reaction. The change of this system in response to treatment of the animal suggests that one of the mechanisms in animals for control of metabolism by alteration of enzyme activities may be analogous to the enzyme adaptation of microorganisms.

This tryptophan oxidizing system could not be found in normal animals until a sensitive assay was available, and was originally demonstrated in the livers of rabbits given tryptophan for the purpose of isolating kynurenine. A low activity can be demonstrated in normal rabbits, but rabbits given 4 g of L-tryptophan the previous day are frequently found to have activities up to ten times those of normal animals. The magnitude and reproducibility of this adaptive increase is shown in Tables 1 and 2. The activity of the system is determined by the formation of kynurenine from L-tryptophan in the supernatant of a fresh liver homogenate provided with adequate amounts of enzyme-generated hydrogen peroxide (*1*). The formyl-kynurenine produced by the coupled oxidation is hydrolyzed to kynurenine by the enzyme formylase. Formylase is present in liver preparations in a 600-fold excess over the coupled oxidation reaction, so that increased kynurenine formation by the system must be due to increased activity of the limiting oxidizing steps. The formylase, measured by an independent method depending upon the hydrolysis of formyl-anthranilic acid (*3*), does not change significantly in preparations showing over tenfold increase in the oxidizing activity (Table 1).

TABLE 1

Treatment	No. animals	μM kynurenine/g Liver/hr		Formylase
		Average ± P.E.	Range	Average ± P.E.
Rabbits				
Normal	9	1.4 ± 0.3	0.90 – 2.10	84 ± 22
5–12 hr after 10 mM DL-tryptophan	10	11.7 ± 1.3	9.60 – 15.30	104 ± 20
15–20 hr after 10 mM DL-tryptophan	8	2.7 ± 0.6	1.80 – 4.20	—
Rats				
Normal	22	1.2 ± 0.2	0.81 – 1.50	—
4–10 hr after 2–4 mM L-glutamic acid, NH_4Cl or DL-alanine	10	1.5 ± 0.3	0.64 – 2.22	—
4–10 hr after 1–2 mM DL-tryptophan	7	8.0 ± 1.8	5.65 – 12.30	—
5–8 hr after 1–2 mM L-tyrosine or L-phenylalanine	4	4.4 ± 0.5	3.84 – 4.56	—
4–8 hr after 2 mM L-histidine	7	9.3 ± 1.4	5.29 – 11.80	—

TABLE 2

Hr after 2 mM L-histidine	No. rats	μM kynurenine/g liver/hr	
2	2	2.3	2.5
4	2	8.4	9.0
5.2	1	11.8	
7.8	2	10.4	11.3
12.5	2	1.9	2.5

Several alternative explanations for this change in the tryptophan oxidizing activity upon tryptophan administration have been tested. The livers of treated and untreated animals are similar in weight and water content. The increased activity after treatment may be demonstrated in liver slices as well as in extracts. The kynurenine formed by the enzyme blanks (without tryptophan) is negligible, even after tryptophan administration to the animal. The enzymes extracted from both types of animals are qualitatively the same. In neither is there evidence of a dissociable co-factor for the system. The activity of a combination of normal plus adapted enzymes is a simple addition of their activities separately. Only liver, and not other tissues, contains the system. The known animal peroxidases from milk and from white blood cells do not augment the reaction of the liver peroxidase system. These observations rule out, as explanations of the increase in activity, various possibilities such as preservation or increased extractability of the enzyme, accumulation of an intermediate, provision of a dissociable co-

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factor, redistribution of enzyme from other tissues, and the presence of a simple inhibitor in normal livers or of a simple activator in treated livers. The final decision as to whether any case of increased enzyme activity is due to a corresponding increase in the amount of enzyme should be based upon an estimation of enzyme concentration not depending upon activity. The evidence so far available suggests, however, that this change in activity of the peroxidase-oxidase system represents an increase of the concentration of the components of this system.

Increased activity of the order shown in the accompanying tables can be produced by oral, subcutaneous, or intraperitoneal administration of tryptophan to rabbits, rats, or guinea pigs. Two characteristics of this reaction may be emphasized. The enzyme increases within several hours after administration of an active substance, and after 15–20 hr has returned to normal. Although the blood levels of administered compounds have not been determined, this close correspondence of enzyme levels to those assumed for any compound administered (e.g., histidine [*4*]), bespeaks a remarkably rapid adaptive response and decline. The time course of this change in the enzyme concentration following the intraperitoneal administration of 2 mM of L-histidine to rats is shown in Table 2. Second, this enzyme adaptation is also produced by several substances that are not substrates for the enzyme, notably histidine and kynurenine and to a lesser extent tyrosine and phenylalanine. Although any physiological connection between these substances and the tryptophan oxidizing system in animals is conjectural at present, the specificity of the enzyme response to them is emphasized by the absence of any response to larger amounts of some other substances administered in the same way.

The mechanism involved in the adaptation of this enzyme in animals would appear to be somewhat complex in comparison to enzyme adaptation in simpler forms. The greater organizational complexity of animals may also provide mechanisms for the increase of enzymes in response to compounds other than their substrates, as part of a general physiological adjustment. Several other enzymes have been found which, though not necessarily adaptive, do have activities different from normal in certain physiological states: succinic dehydrogenase (*5, 6*), cytochrome *c* (*7*), proline oxidase (*8*), arginase (*9*), alkaline phosphatase (*10*), and xanthine oxidase (*11*). The more immediate implications of this particular response concern its undoubted effect upon the amount of tryptophan converted to kynurenine and other metabolites *in vivo* (*12*), and its possible role in determining the amount of tryptophan converted to nicotinic acid under various conditions (*13*).

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Experiments on the Catalytic Exchange of Acetone and Propane with Deuterium

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The reduction of acetone to propane with deuterium on platinized platinum was attempted at low temperatures (−20° C) in an effort to prepare $CH_3CD_2CH_3$ as predicted by Farkas and Farkas (*1*). It was hoped that the electron dissociation pattern of this compound would aid in the interpretation of the results of the mass spectrometric examination of the exchange of propane with deuterium.

The experimental method was similar to that used by Farkas (*1*). The catalyst was prepared by platinizing a platinum electrode in the standard manner, using a 3% solution of platinic chloride and .02% lead acetate. It was washed with boiling water, rinsed with acetone, and dried by a stream of nitrogen. In order to prevent contamination by stopcock grease and mercury vapor the catalyst was never kept *in vacuo*. The catalyst was found to remain stable for periods as long as 2 weeks if left in an atmosphere of nitrogen or hydrogen when not in use.

Approximately 7 cm of acetone was admitted to the reactor and frozen with dry ice, after which about 14

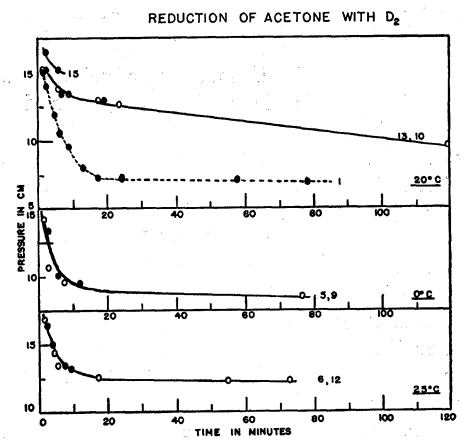

FIG. 1.