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SOME BIOCHEMICAL STUDIES ON CERTAIN TRYPTOPHAN METABOLITES IN TUBERCULOUS GUINEA PIGS

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Tryptophan and some indole derivatives proved to be tuberculostatic both *in vitro* and *in vivo*[2)~5)]. Indole, in therapeutic doses was effectively tuberculostatic in guinea pigs and human beings[2)5)]. Indole acetic and indole-propronic acid were less effective as tuberculostatic agents. Skatol had also a tuberculostatic effect both *in vitro* and *in vivo*, but in large therapeutic doses it was toxic to mice which limited the experiment.

Some indole compounds have been found to increase in blood and urine of tuberculous patients and to diminish as a metabolic consequence to treatment with traditional antituberculous drugs[7)10)18)22)23)].

This work was therefore conducted to study the metabolism of some indole compounds in tuberculosis, namely serum total indoles and blood serotonin level, in tuberculous guinea pigs.

EXPERIMENTAL

The guinea pigs were selected from the laboratory stock. For this purpose 54 guinea pigs of the male sex, weighing from 250 to 300 g were selected and kept on a stock diet of rye and green clover during the experimental period. Each 9 animals were separately kept in a cage. 27 guinea pigs were kept as normal controls. The other 27 guinea pigs were infected by subcutaneous injection of 0.001 mg of mycobacterium tuberculosis hominis type $H_{37}Rv$. A group of nine animals each of the control and infected were sacrificed after 15, 30 and 52 days of infection. The animals were sacrificed by decapitation after an overnight fast and blood was collected. Blood was analysed for serum total indoles[18)] and blood serotonin[12)]. The success of infection was proved at autopsy by demonstrating the acid fast bacilli, in the animals' liver, spleen and regional lymph nodes according to the method of Feldman and Hinshaw (1945).

RESULTS

Serum total indoles and blood serotonin level, in normal and tuberculous guinea pigs during experimen-

	Normal guinea pigs			Infected guinea pigs		
	Days			Days		
	15	30	52	15	30	52
Serum total indoles*						
Mean	16.00	15.86	16.4	17.11	17.44	22.33
St. D.	±1.32	±1.2	±1.3	±2.9	±2.8	±2.85
St. E.	±0.45	±0.42	±0.46	±0.9	±0.9	±0.95
P	—	—	—	>0.05	>0.05	<0.05
Blood serotonin*						
Mean	0.477	0.482	0.490	0.497	0.500	0.584
St. D.	±0.05	±0.05	±0.05	±0.05	±0.03	±0.1
St. E.	±0.01	±0.01	±0.013	±0.013	±0.01	±0.03
P	—	—	—	0.05	0.05	0.05

* The values are the mean of 9 samples.

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tal period ($\mu g/ml$).

There was a gradual increase in the level of total indoles and secretion which was proportional with the duration of infection. During the first month of tuberculous infection, the increase was statistically insignificant as compared to the normal controls. After 52 days, tuberculous animals showed significant increase in serum total indoles and blood serotonin levels.

Discussion

Normally the levels of the indole compounds in blood are kept constant by different specific homeostatic processes[17)20)]. In tuberculous guinea pigs the indole compounds, represented in this work by total indoles and blood serotonin, were elevated. The rise was proportional to the duration of infection, and to the extent of the lesions. This biochemical result is comparable to that found in tuberculous patients (Stepanian[22)23)], Mastennikova[18)] and Abdel Kader et al.[7)10)]).

The biochemical genesis of this rise may be attributed to more than one factor. Destruction of tissue proteins accompanied by degradation into amino acids including tryptophan and its indole derivatives. Hormonal imbalance could another predisposing factor causing the pathological rise of blood indoles. Insulin overactivity was proposed to be present in tuberculous nondiabetic patients[6)8)]. Suprarenal insufficiency was also found to be present in individuals suffering from tuberculous infection[1)11)16)21)]. These two factors, insulin overactivity and suprarenal insufficiency, might be also the responsible factors for the apparent increase in indole compounds in blood. Insulin overactivity was found to increase plasma tryptophan by releasing it from the liver[24)]. Glucocorticoids were found to potentiate the action of tryptophan pyrrolase[14)] which destroys the indole ring, hence tending to deviate the enzymatic metabolic transformation of tryptophan from the indole pathway.

The outcome of the increase in indole derivatives in tuberculosis could be a probable biochemical defence mechanism against the invading mycobacterium as proved by Abdel Kader et al.[2)~5)].

Further work is in progress to clarify the role of indole compounds in tuberculosis.

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