Tab. II. Analysis of variance

Source of variation	Degrees of freedom	Deviance	Variance	F	Critical values of F for $P < 0.01$
Between asthmatics and non-asthmatics	1	19855.00	19855.00	37.32	6.76
Between before and after 48/80	1	29418.47	29418.47	55.30	6.76
Interaction	1	0.53	0.53	0.000996	6.76
Experimental error	216	114906.00	531.97	—	—
Total	219	164180.00	—	—	—

The results reported in Table I show that this average number was higher in non-asthmatics (73.11) than in asthmatics (54.15) with a percentage of degranulated cells respectively 44.19% and 73.71%. After treatment with the histamine liberator 48/80, the average number of mast cells decreased both in non-asthmatics (50.02) and in asthmatics (30.98); the percentage of degranulated cells rose in both groups (non-asthmatics: 58.92%; asthmatics: 87.44%).

The significance of the data thus obtained was verified using the *variance-ratio F test.* As shown in Table II, it is practically certain that the diverse distribution of mast cells in the two groups of patients is due to systematic factors connected with bronchial asthma. The F value was in fact greater than the value corresponding to $P < 0.001$: the probability of a casual divergence between the average numbers of mast cells in asthmatics and in non-asthmatics is therefore lower than one per thousand. The difference between the average numbers of mast cells before and after treatment was also still significant at the level $P < 0.001$. A higher reactivity of mast cells to the compound 48/80 in asthmatics was, on the other hand, excluded with practical certainty by probabilistic analysis ($F = 0.000996$).

This study confirms the findings of our previous work, i.e. that the numerical reduction and the degranulation of mast cells are a characteristic phenomenon of the hyperergic-patergic reactivity of bronchi in asthmatics; these alterations are absent, or of much lower intensity, in normergic inflammation characteristic of non-asthmatic bronchitis.

The reliability of these conclusions is supported by the rigorous method applied. The significance of sampling is validly proved by its homogeneity: in fact, on drawing a frequency distribution curve of the quantities of mast cells, a nearly perfect Gaussian curve was obtained[5].

Riassunto. Lo studio comparativo dei mastociti bronchiali in 2 gruppi di pazienti: (1) bronchitici non-asmatici, (2) asmatici, dimostrò che in questi ultimi le «Mastzellen» erano meno numerose e prevalentemente degranulate. Il 48/80 produsse nei 2 gruppi diminuzione cellulare e degranulazione. Il *test F* dimostrò l'alta significatività dei suddetti reperti, mentre esluse una interazione tra asma e reazione al farmaco.

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Effect of Dibenzyline on Serum Cholesterol in Rabbits[1]

Much interest has been shown in the hormonal regulation of lipid metabolism. Amongst other problems which have received attention, is that of the influence of sympathomimetic drugs on serum cholesterol. Animals treated with adrenalin or serotonin show often an increased level of serum cholesterol[2–6]. On the other hand, it has been reported that some ganglion blocking agents, used for treatment of hypertension, not only lower blood pressure but also depress the level of serum cholesterol[7,8]. Our experiments on rabbits with adrenergic substances (serotonin and nor-adrenalin) and with a ganglion blocking substance (Dibenzyline), gave different results in short term tests. In view of this discrepancy the following observations are believed worth reporting.

Method and Results. In the present experiments adult healthy rabbits of either sex were used. Nor-adrenalin bitartarate was given intramuscularly, 0.6 mg in an aqueous solution once a day for 2 days to 26 rabbits. 20 mg of serotonin were given intramuscularly to 12 animals in an aqueous solution of 5-hydroxytryptamine creatinine sulfate once a day for 2 days. Dibenzyline (N-phenoxyisopropyl-N-benzyl-β-chlorethylamine hydrochloride, Smith, Kline & French Labs., Phila.) in doses of 2.5 mg/kg of body weight was injected into the ear vein of 17 animals. The intravenous injections were given slowly, over periods of 20 min. When signs of blocking appeared (as hypersalivation, enophthalmos, etc.), the speed of the injection was still more decreased. Notwithstanding this precaution, all the animals were weak and listless at the end of the injection, but recovered within 2 h. One rabbit died during the injection, and one other rabbit showed

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serious symptoms of adrenergic blockade after the administration, but recovered within 6 h. Blood was taken before and 24 h after injection and serum cholesterol was estimated by the SPERRY-WEBB method[9].

The serum cholesterol decreased slightly after administration of nor-adrenalin (mean: -3.6%, $p < 0.02$), and the change of cholesterol by the serotonin treatment was not significant. However, 24 h after single i.v. injections of Dibenzyline the serum cholesterol increased and that to a highly significant degree (Table).

Discussion. Like a number of other adrenergic blocking agents, Dibenzyline produces its effect by reducing the pressor action of adrenalin. From numerous investigations which showed that adrenalin elevates the serum cholesterol level, its seemed reasonable to assume that any anti-adrenergic agent will lower the cholesterol level and indeed there are reports that serum cholesterol decreases after administration of some ganglion blocking drugs[7,8,10]. Contrarily, I have found that in short-term experiments on rabbits, an adrenergic blocking substance, namely Dibenzyline, has a cholesterol raising effect. There is only one investigation in which the influence of Dibenzyline on serum cholesterol was studied: Hollister reported that Dibenzyline lowers serum cholesterol, but the statement was based on tests in only 2 patients, one of which showed an equivocal decrease. Moreover, this author's tests were carried over several weeks, and as he himself indicated, not with sufficient dosage. For these reasons, the results are not comparable.

The explanation why Dibenzyline failed to decrease the level of serum cholesterol and even raised it, presents difficulties. According to recent reports[11,12] on the action of adrenalin, the mobilization of lipids from tissue to serum is controlled by adrenalin. However, according to data which we obtained, neither nor-adrenalin nor serotonin which have adrenergic action always raise serum cholesterol levels in rabbits.

Furthermore the weakness of the animals after injection of Dibenzyline has to be considered as having a possible effect on cholesterol metabolism and thus may counteract an hypothetical specific serum cholesterol lowering effect of Dibenzyline. This weakness may be considered an expression of stress which is said to have some effect on cholesterol metabolism[13,14]. However. this effect is very inconsistent in animals and humans. Nevertheless, such possibility of interference should not be overlooked. It therefore remains to be established whether Dibenzyline has a direct action on serum cholesterol preventing its catabolism, which is unlikely; whether the rise in cholesterol is due to vascular phenomena, or whether a metabolic disturbance is responsible.

5.0 ml of 0.5 mg per ml aqueous solution of Dibenzyline per kg body weight were administered intravenously

Rabbit	Sex	Body weight g	Cholesterol in mg% before test	Cholesterol in mg% after test	% change
1	M	4930	27	37	+ 37.0
2	M	2370	32	38	+ 18.7
3	M	3680	33	41	+ 24.2
4	M	2510	38	48	+ 26.3
5	M	2190	43	48	+ 11.6
6	F	2250	48	63	+ 31.3
7	M	3240	63	64	+ 1.6
8	F	2500	82	107	+ 30.4
9	M	3320	86	76	−11.6
10	M	2600	88	97	+ 10.2
11	M	3140	98	118	+ 20.4
12	F	2010	104	109	+ 4.8
13	F	2750	104	125	+ 20.2
14	M	3830	135	161	+ 19.2
15	M	2910	180	196	+ 8.9
16	F	2820	186	175	− 5.9
17	F	4390	371	308	−17.0
				mean	+ 13.5

$t = 3.6$, $p < 0.01$

No. 1: very weak, hypersalivation and enophthalmos after injection.

Zusammenfassung. Im Gegensatz zu den Beobachtungen, die zeigten, dass adrenergische Substanzen Serumlipoide einschliesslich Serumcholesterin erhöhen, wird in kurzfristigen Versuchen an Kaninchen eine etwas unregelmässige Senkung des Serumcholesterins nach Injektion von Noradrenalin und keine signifikante Beeinflussung des Serumcholesterins nach Injektion von Serotonin gefunden. Dibenzylin erhöhte in kurzfristigen Versuchen das Serumcholesterin ausgesprochen signifikant.

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The Effect of pH on Enzymatic Formation and Inhibition of Norepinephrine Synthesis

The extraction and purification of an enzyme from adrenal medulla which catalyzes the conversion of dopamine to norepinephrine was recently described[1]. It was shown that this enzyme is non-specific and also catalyzes the conversion of other phenylethylamines and phenylpropylamines to the corresponding β-hydroxy compounds[2,3]. In view of these findings, the enzyme was named phenylamine-β-hydroxylase[3].

The present communication is concerned with the effect of pH upon the rate of conversion of dopamine to norepinephrine and epinine to epinephrine by phenylamine-β-hydroxylase. The effect of pH on the inhibition rate of dopamine to norepinephrine conversion by various inhibitors was also examined.

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