the different agents, namely light and aflatoxin B_1, acting on the same tissue served a similar mode of reaction. Although a possible limitation of the availability of the co-factors, either ATP or CoA to retain the precursor synthesis caused by the presence of aflatoxin B_1 in skin is not eliminated, the binding of aflatoxin with some proteins[12,13] and its inhibition of some enzyme activity[14] may suggest its interaction with acetate thiokinase (EC. 6.2.1.1.) and thus, results in the observed inhibitory effect[15].

Table II. Effect of aflatoxin B_1 on the incorporation of ^{3}H-acetyl CoA into human skin lipids[a]

Fraction	Experiment		
	Control	Aflatoxin (dpm/100 mg wet wt.)	Change (%)
Total lipids	5,570	5,240	−5.4
Polar lipids	1,767	1,800	+1.9
Free fatty acid	845	799	−5.4
Free sterols	871	954	+9.5
Glycerides	771	774	+0.3
Sterols esters	771	745	−3.4

[a] Details were described in ref.[11]

Zusammenfassung. Aflatoxin B_1 hemmt den Einbau von 1-^{14}C-Azetat in die Lipide der menschlichen Haut. Wird aber ^{3}H-Azetyl-CoA als Vorstufe für den Lipideinbau verwendet, so kommt es zu keiner merklichen Hemmung. Die Azetataktivierung scheint somit die wichtigste, vom Toxin beeinflussbare Stufe der Lipidsynthese zu sein.

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Antrectomy Prevents Nicotine from Activating Rat Stomach Histidine Decarboxylase

The activity of rat stomach histidine decarboxylase seems to vary with the serum gastrin level[1]. Nicotine has been reported to cause activation of the enzyme[2]. This effect may be a direct one, elicited in the enzyme-containing cell itself, or an indirect one, mediated by nicotine-induced release of gastrin from its storage site in the antrum[3]. If the enzyme activation seen after administration of nicotine is mediated by gastrin, antrectomized rats should not respond.

Adult male albino rats (Wistar strain, 150–200 g body weight) were used. Antrectomy was performed by resection of the distal half of the glandular stomach (the pyloric gland area together with the adjacent portion of the oxyntic gland area) and the duodenal bulb[4]. Gastrointestinal continuity was re-established by gastro-duodenostomy end-to-end. Operated rats were allowed to recover for at least 3 weeks before they were used in experiments. Nicotine (0.2–5 mg/kg) was given s.c. in a single dose. If not otherwise stated the rats were killed 2 h after injection. Controls received saline. All rats were fasted for 48 h (free access to water) before sacrifice. They were killed by decapitation under light diethyl ether anaesthesia. The stomachs were taken out, cut open along the major curvature and washed with ice-cold 0.9% saline. The mucosa was scraped off the oxyntic gland area, homogenized in 0.1 *M* phosphate buffer, pH 6.9 (final tissue concentration 100 mg wet weight per ml) and centrifuged at $10{,}000 \times g$ for 15 min at 0 °C. Enzyme activity was measured as $^{14}CO_2$ produced from 1-^{14}C-L-histidine[4,5]. The reaction mixture (0.5 ml) contained 0.4 ml of the supernatant, 10^{-5} *M* pyridoxal-5′-phosphate,

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Table I. Effect of nicotine on the activity of rat stomach histidine decarboxylase (dose-response relationship)[a]

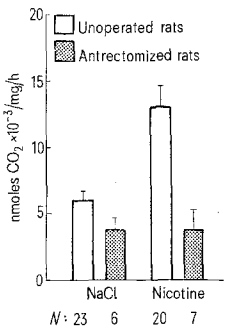
Nicotine (mg/kg)	Histidine decarboxylase activity (nmoles $CO_2 \times 10^{-3}$/mg/h) mean ± S.E.M. (*n*)	
0	6.3 ± 0.7 (23)	
0.2	13.7 ± 1.5 (17)	$P < 0.001$
1.0	12.8 ± 1.6 (20)	$P < 0.001$
5.0	5.8 ± 1.2 (16)	

[a] The rats were killed 2 h after injection.

Table II. Histidine decarboxylase activity at various times after administration of 0.2 mg/kg nicotine

Time (h)	Histidine decarboxylase activity (nmoles $CO_2 \times 10^{-3}$/mg/h) mean ± SEM (*n*)	
0	6.3 ± 0.7 (23)	
1/2	4.0 ± 1.1 (5)	
1	8.1 ± 2.5 (5)	
1 1/2	13.8 ± 3.6 (5)	
2	13.7 ± 1.5 (17)	$P < 0.001$

5×10^{-4} *M* glutathione and 4×10^{-4} *M* 1-^{14}C-L-histidine (1.3 mC/m*M*) added in this order. The mixture was gassed with nitrogen for 5 min at 0 °C. After 1 h at 37 °C the reaction was terminated by the addition of 0.5 ml 10% trichloroacetic acid and the evolved $^{14}CO_2$ was trapped during 30 min at 37 °C on a filter paper strip, previously immersed in Protosol® and placed in a central well in the reaction vessel. The radioactivity was then determined in a liquid scintillation spectrometer. The results were corrected for non-enzymatic decarboxylation by incubating identical samples with 1-^{14}C-D-histidine instead of 1-^{14}C-L-histidine. Duplicate assays were run in all experiments.



The nicotine-induced activation of rat stomach histidine decarboxylase is prevented by antrectomy. Nicotine: 0.2 mg/kg. Controls received 0.9% saline. The rats were killed 2 h after the injection. Enzyme activities are expressed as nmoles CO_2 produced per mg tissue and hour. *N* denotes the number of rats in each group.

Single injections of 0.2 or 1 mg/kg of nicotine caused activation of gastric histidine decarboxylase in normal, fasted rats, whereas a dose of 5 mg/kg failed to raise the enzyme activity (Table I). The enzyme activity seemed to reach a peak $1^1/_2$–2 h after administration of nicotine (Table II). Antrectomy prevented the nicotine-induced enzyme activation (Figure). It may thus be suggested that nicotine activates gastric histidine decarboxylase through the release of gastrin. The results do not support the alternative explanation that nicotine has a direct effect on the enzyme-containing cells.

Zusammenfassung. Nikotin steigert die gastrische Histidindekarboxylasaktivität in normalen, nüchternen, nicht aber in antrektomierten Ratten. Dieses weist darauf hin, dass die Aktivierung durch nikotininduzierte Freisetzung von antralem Gastrin verursacht wird.

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The Bohr Effect and the Red Cell 2-3 DPG and Hb Content in Sherpas and Europeans at Low and at High Altitude

In a previous paper[1] we have reported that the Bohr effect of individuals of Amerindian origin living in the highlands of Peru was significantly higher than that of Europeans living at the same altitude and we have interpreted this difference as the effect of an evolutionary adaptation to life at low oxygen pressure.

The aim of the present research was 1. to ascertain whether in a different population, living at an altitude comparable with that of the Peruvian population, the same adaptation has occurred; 2. to collect more data on Europeans in order to know if physiological phenomena of adaptation resulting into an increase of the Bohr effect can also occur in Caucasian individuals.

Materials and methods. Four types of individuals were examined: 1. Sherpas living at high altitude; 2. Sherpas living at low altitude; 3. Europeans at high altitude and 4. Europeans at low altitude.

The research has been carried out in Nepal in October 1970. The high altitude samples were taken at 4950 metres above the sea level, in the region of Solo Khumbu, from 24 porters of the expedition and 12 members of an Italian alpinistic team. The bleedings were done after staying for three to four days at that altitude.

The low altitude Sherpa samples were obtained from a group of Sherpas of the region of Helambu, (about 3500 metres above the sea level) but living in Kathmandu (1200 metres above sea level)[2]. The European samples at low level were obtained from the same alpinistic team in Italy before the departure of the expedition.

The oxygen dissociation curves were determined in Rome by a previously described spectrophotometric technique[3] on airshipped hemolysates prepared and reduced with nitrogen in the field (previous experiments have shown to us that the oxygen affinities of reduced hemolysates is stable for months).

The haemoglobin content per ml of whole blood was determined by the cyanmethaemoglobin method[4]. The red cell 2–3 DPG was determined according to BARTLETT[5] on hemolysates whose 2–3 DPG was stabilized by boiling the specimens diluted in distilled water. All the hemolysates were also examined by starch gel electrophoresis according to GOLDBERG[6] and only normal haemoglobin (A + A_2) were detected.

Results and discussion. The results are shown in detail in Tables I and III and their comparisons are shown in Table IV.

Table I shows the data concerning the Europeans at low and high altitude. The Bohr effect and mean Hb content of the 2 samples of Europeans are not significantly different from each other (see Table IV). However, some interesting intracouple (subjects No. 5, 9 and 12) difference is apparent (the intracouple data refer to those subjects who were tested both at low and at high altitude).

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