Since the molecular weight of the active pepsin (below pH 6.0) is about 34,000, it would appear that the inactivation process which occurs between pH 6.75 and 7.25, is accompanied by a dimerization of the active subunit.

From the experiments reported above, it appears that the loss of the catalytic property of the enzyme parallels the gradual conversion of the active monomer into an inactive aggregate. Further analysis of this process is now in progress by using sucrose density gradients centrifugation and disc-electrophoresis[11].

Riassunto. A bassa temperatura (5 °C) variando il pH del mezzo da 6,50–7,25, la pepsina varia le sue dimensioni molecolari e si inattiva. Tale fenomeno, evidenziato per gel filtrazione, sembra sia dovuto alla formazione di un aggregato della pepsina di peso molecolare molto vicino a quello dell'albumina bovina.

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Metabolism of Alcohol in Partially Hepatectomized Rats Exposed to Cold

Several workers have shown that cold exposure in rats resulted in an increased oxidative activity of the liver[1–6]. WEISS and MOSS[5] reported that the liver, an organ which has one of the lowest metabolic rates among several tissues, showed the greatest metabolic increase in response to cold. The latter authors also have shown that the metabolic rate of liver slices in partially hepatectomized rats increased 20% when animals are kept at room temperature and slightly over twice this amount when exposed to a cold environment.

Earlier we reported that rats exposed to cold, metabolized alcohol faster than controls kept at room temperature[7]. In the present experiment, we have determined the effect of partial hepatectomy on the ability of cold exposed and room temperature housed rats to metabolize alcohol[8].

Methods. Male albino rats of Sprague-Dawley strain weighing 190–210 g were divided into 6 groups of 10 rats/group. The first 3 groups consisted of partially hepatectomized, sham-operated, and non-operated control animals which were placed in a cold room at a temperature of − 5 °C, 48 h after surgical intervention where they remained for a period of 5 days. The other 3 groups, divided and operated upon as above were kept at room temperature (20° ± 2 °C) for 7 days. On the eighth post-operative day each animal received i.p. 0.8 g/kg of uniformly labelled ^{14}C-alcohol (specific activity 0.23 μC/mM of alcohol) as a 20% aqueous alcohol solution. Respiratory $^{14}CO_2$ was collected by the method described previously[7]. Partial hepatectomy was performed as described by HIGGINS and ANDERSON[9].

Analysis of variance was performed with an IBM computer, Model 650, according to the 'R × 2 Tables' of YATES[10].

Results. The most striking difference in $^{14}CO_2$ recovery occurred during the first 3 h following alcohol administration (Table I). During this time, all animals exposed to cold metabolized as much alcohol as the room temperature-housed rats oxidized in 9 h. The effect of temperature on the recovery of labelled carbon dioxide was

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Table I. Mean values of cumulative recoveries of exhaled $^{14}CO_2$ (mM) from metabolized alcohol

Treatment	Interval of CO_2 collection				
	1 h	3 h	5 h	7 h	9 h
Control, room temperature	0.71	3.60	4.42	4.70	4.86
Control, cold	1.30	4.83	5.32	5.49	5.57
Sham, room temperature	0.78	3.52	4.50	4.80	4.95
Sham, cold	1.36	4.84	5.44	5.64	5.73
Partial hepatectomy, room temperature	0.63	3.23	4.30	4.58	4.73
Partial hepatectomy, cold	1.33	4.70	5.16	5.39	5.47
F of effect of temperature	31.98[a]	39.37[a]	35.09[a]	31.09[a]	28.48[a]
F of treatment	0.26	0.53	0.55	0.85	1.02

F of effect of treatment = 9.18[a]; F of effect of temperature = 0.37. [a] $P < 0.01$.

Table II. Specific activity of $^{14}CO_2$, expressed as number of cpm/mM of expired CO_2

Treatment	Interval of CO_2 collection				
	1 h	3 h	5 h	7 h	9 h
Control, room temperature	3829	7851	2291	762	424
Control, cold	3839	4980	770	241	130
Sham, room temperature	3807	8420	2923	973	521
Sham, cold	4066	5339	837	296	148
Partial hepatectomy, room temperature	2907	7255	2708	813	423
Partial hepatectomy, cold	3817	4916	708	221	118
F of effect of temperature	3.58	32.85[a]	28.91[a]	31.34[a]	35.13[a]
F of treatment	2.77	0.88	0.34	0.63	0.47

F of effect of treatment = 9.18[a]; F of effect of temperature = 0.37. [a] $P < 0.01$.

Table III. Mean values of liver weight (g) at autopsy

Treatment	Room temperature	Cold-exposed
Non-operated control	9.92	9.34
Sham-operated	8.58	9.31
Partial hepatectomy	7.58	6.70

F of effect of treatment = 9.18[a]; F of effect of temperature = 0.37. [a] $P < 0.01$.

statistically significant ($P < 0.01$) at each collection period. However, no difference appeared at any stage of the experiment within the groups kept in the cold or at room temperature.

On the other hand, except during the first hour, rats kept at room temperature exhaled significantly ($P < 0.01$) more $^{14}CO_2$ in proportion to the total quantity of exhaled carbon dioxide than those maintained in the cold (Table II). No difference was observed between treatments at either temperature of exposure.

No attempt was made to correlate the weight of the livers at autopsy and rate of recovery of $^{14}CO_2$. In cold-exposed animals, the liver weight of the partially hepatectomized rats was significantly ($P < 0.01$) below that of the control groups. Rats exposed to cold lost weight, whereas all groups at room temperature gained in weight. Hepatectomy had no significant effect on body weight (Table III).

Discussion. It is known that the increased capacity of the cold-exposed rat to produce heat is reflected in an elevated in vitro oxygen consumption of certain tissues such as the liver[1-3]. However, WEISS has shown that the various tissues of the body do not acclimatize at the same rate. The liver seems to be the first tissue to increase its rate of oxygen consumption, although skeletal muscles also increased their oxygen consumption through shivering.

In the present experiment exposure of rats to acute cold resulted in an elevated metabolism of ethyl alcohol. This was particularly pronounced during the first 3 h when the greatest portion of the alcohol was metabolized; but the relative metabolism of alcohol, as measured by the specific activity of $^{14}CO_2$, was depressed in all groups of animals exposed to cold. WEISS and MOSS[5] reported that cold environment does not interfere with the rat's ability to regenerate the liver mass. This was confirmed in the present experiment.

PETERS, KRIJNEN and MCEWEN[11] found that weight regeneration of the liver was almost complete 4–6 days after hepatectomy. Further, the activity of the regenerated liver, as measured by reduction in pentobarbital induced sleeping time had returned to normal by the seventh to ninth day following hepatectomy. FOUTS, DIXON and SHULTICE[12] found that activity of several drug metabolizing enzymes in the rat liver returned to normal in 4–10 days after partial hepatectomy. In the present experiment, while liver weight regeneration in the hepatectomized animals was not complete at termination on the eighth post-operative day, the activity of the alcohol detoxification system, as measured by recovery of exhaled $^{14}CO_2$ derived from labelled ethanol, did not differ significantly from the sham-operated and non-operated control animals. Regeneration of liver mass and activity were not adversely affected by acute exposure to cold.

The increased metabolism of alcohol by the liver of cold-exposed rats might be a measure of the increased over-all metabolic rate of this organ; it metabolized all substrates more rapidly, including alcohol. However, when the contribution of alcohol to the general metabolism of the whole animal is determined (specific activity), it is decreased as compared to room temperature controls. This would confirm the conclusion of other workers, to the effect that tissues other than the liver contribute little to the metabolism of alcohol[13].

Résumé. Le taux de conversion de ^{14}C de l'alcool au $^{14}CO_2$ respiratoire aussi bien que l'activité spécifique du $^{14}CO_2$ fut différent entre des rats partiellement hépatectomisés, des opérés à blanc et des témoins absolus exposés au froid et leurs témoins maintenus à la température du laboratoire. Toutefois, aucune différence ne fut observée à l'intérieur même des groupes exposés au froid, ni chez ceux maintenus à la température du laboratoire.

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