glucose, FFA and ketones, while in streptozotocin diabetes there is hyperglycemia but plasma FFA and blood ketones are not significantly elevated[8]. On the other hand, our results are in agreement with those of ALTSZULER et al.[11] in dogs. Therefore it is evident that decreased lipolysis by DBA can occur in the absence of increased insulin secretion.

Up to now, the only antilipolytic hormones known are insulin and prostaglandins: since we must reject the hypothesis of insulin being responsible for the DBA antilipolytic effect observed in vivo, we might consider the hypothesis of a prostaglandin-like substance. Ho et al.[12] observed that a hormone antagonist is formed in fat cells during hormone action; the effect of this antagonist can be mimicked by prostaglandin E_1 and E_2[12]; moreover prostaglandins are released from adipose tissue in response to hormonal stimulation[13].

Since both cAMP and DBA mimicked the action of hormones to promote antagonist formation[12], it seems likely that antilipolysis by DBA in vivo might be due to excessive production of the antagonist itself which might therefore be able to overcome the direct action of the low concentrations of cyclic nucleotides which can reach fat cells in vivo.

Riassunto. La somministrazione di DBA a ratti sia normali che resi diabetici con streptozotocin provoca un persistente effetto antilipolitico, indipendente dai valori di insulina plasmatica.

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Pentobarbital Anaesthesia. Effects on Blood Sugar, Serum Immunoreactive Insulin and Free Fatty Acid Responses to Glucose[1]

These studies were made in dogs, basally and during an intravenous glucose tolerance test.

Material and methods. 7 male and 1 female mongrel dogs, weighing 9–16.3 kg, fed on dog chow pellets and water ad libitum were used. After 17–22 h fast, they were anaesthetized (sodium pentobarbital, 33 mg/ml aqueous solution, 1 ml/kg body wt., rapid i.v. injection). Tests were performed 1 h later; glucose was rapidly injected in femoral vein (1 g/kg body wt., 20% aqueous solution), and blood was withdrawn (femoral vein) at several intervals thereafter. Control experiments using unanaesthetized dogs were carried out (self-control design).

Blood samples were assayed for blood sugar (BS) (Technicon Autoanalyzer[2]), both serum immunoreactive insulin (IRI)[3] and free fatty acids (FFA)[4]. All results were analyzed for variance[5].

Results. As shown in the Figure, BS, serum IRI and FFA basal levels remained unaffected by anaesthesia.

The BS peak during the test in the unanaesthetized dogs was higher than in controls ($p < 0.001$ between 5 and 25 min, $p < 0.01$ at 45 min). Glucose disappearance from blood during the test followed an exponential law in unanaesthetized dogs, as shown by a high, highly significant correlation coefficient for the relationship shown in the Table. Previous reports were thus confirmed[6]. The law followed in anaesthetized dogs was also exponential and similar in slope, but their y means differed (see Table). Therefore, glucose space appeared to be modified by pentobarbital.

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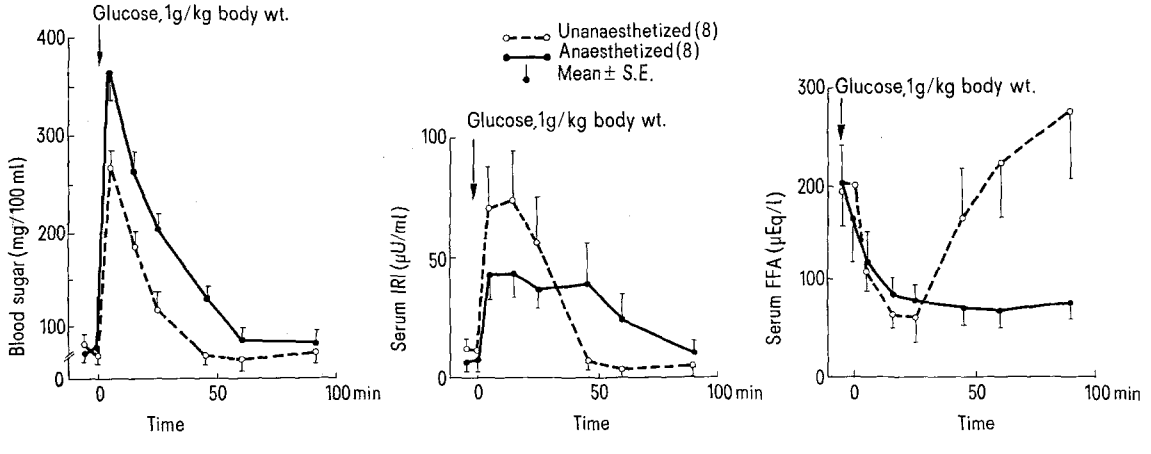

Some effects of pentobarbital anaesthesia. Number of animals per group in parenthesis.

Influence of pentobarbital-induced anaesthesia on blood sugar levels during an i.v. glucose tolerance test in dogs

Dogs	Unanaesthetized	Anaesthetized
Correlation coefficient (r and Pr)	−0.80 (0.001)	−0.87 (0.001)
Error of estimation of r	0.15	0.15
$y=\log_e BS=a+kt$	$\log_e BS=5.3251-0.0154t$	$\log_e BS=5.7890-0.0180t$
Slope (k)	−0.0154	−0.0180[a]
Error of estimation of k	0.0016	0.0014
y mean	4.7106	5.0675[b]
Error of estimation of y mean	0.0460	0.0404

Glucose dose: 1 g/kg body wt. Semilog relationship of BS levels (mg/100 ml) to time after glucose injection (min) was analyzed. Statistical analysis according to BANCROFT[7], except for estimations of y means and k, and respective errors[8]. [a] N.S.; [b] $p < 0.001$. Comparisons respect to unanaesthetized controls, Student's t-test[8].

The insulin response to glucose in the anaesthetized dogs was lower and more maintained than in the controls (Figure). The serum IRI peak was 50% lower ($p < 0.05$ at 5 and 15 min from glucose load) but serum IRI at 45 min, still above base line, was 5-fold above the value found in unanaesthetized dogs.

Pentobarbital anaesthesia, although it only moderately delayed the initial fall of serum FFA levels following glucose load, definitely impaired their rebound at the end of the test (Figure). The fall was significant at 15 and 25 min ($p < 0.05$) in the controls, while it was significant just at 45 and 60 min ($p < 0.05$) in anaesthetized dogs. Circulating FFA levels of the dogs in both conditions significantly ($p < 0.01$) differed at 60 and 90 min.

Discussion. Barbiturates appear not to affect the BS basla levels, as observed in dogs receiving amytal[9] and in rats given pentobarbital[10]. Our results reported in the present paper are in agreement with these findings, as well as with the alterations in BS curve during glucose tolerance tests induced by amytal[9], barbital and thiopental[11]. According to our observations, dogs receiving pentobarbital appear to be more tolerant to glucose than rats in the same condition[10], as demonstrated by unaltered glucose disappearance rate from circulation.

Our results reported in this peper clearly indicate that pentobarbital anaesthesia definitely reduces the insulin levels achieved after glucose load, in spite of inducing a higher degree of hyperglycaemia and, also, in spite of lacking any direct action on insulin secretion[12].

It is difficult to find a sole mechanism to explain all the effects of pentobarbital-induced anaesthesia on the 3 parameters studied by us. DAVIDSON[10] postulated that, in rats, pentobarbital-induced glucose intolerance is exerted by waff of growth hormone. According to our comparative study, however, this mechanism fails to explain the alterations of both serum IRI and FFA curves exerted by the barbiturate. Thus, the stimulatory effect of growth hormone on insulin secretion[13] and its lipomobilizing action in vivo in dogs[14] are well known. Since catecholamines were reported to depress insulin secretion[15], the predominant α-adrenergic tone found in dogs given barbiturates[16] might explain the reduction in serum IRI peak. The lack of rebound of serum FFA levels at the end of the test disagrees with this hypothesis, however, and appears to be related to prolonged hyperinsulinaemia.

Conclusion. The present paper emphasizes the need for a careful reexamination of results obtained from experiments using pentibarbital in metabolic studies.

Resumen. En este trabajo se demuestra que la anestesia con pentobarbital provoca modificaciones en los niveles de glucemia, insulinemia y ácidos grasos libres circulantes alcanzados durante pruebas de hiperglucemia provocada con glucosa, por lo que resulta aconsejable ser cauto en la interpretación de resultados de estudios metabólicos que impliquen la medición de estos parámetros en animales así anestesiados.

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