3 × cristallisée, d'origine porcine (Calbiochem.) Les résultats entre les groupes ont été comparés par la méthode de l'analyse de variance[21].

Résultats. Nous pouvons observer sur le Tableau I que les paramètres de sécrétion (volume, débits acides, débit peptique) et d'irrigation (FSMG) sont tous modifiés si on les compare globalement, avec un seuil de signification qui varie de $p < 0{,}05$ à $p < 0.001$; les plus larges variations portent sur le volume du suc, son débit peptique et sur l'irrigation de la muqueuse sécrétante. Par contre, l'efficacité sécrétoire calculée, c'est-à-dire la quantité de sang nécessaire à la sécrétion de 1 ml de suc, de 100 µEq d'acide ou de 1 mg de pepsine, ne subit aucune variation globale statistiquement significative ($F < 2{,}77$), même si parfois les fluctuations paraissent importantes d'un groupe à l'autre.

Sur le Tableau II, nous avons porté les valeurs de F pour une comparaison inter-groupe lorsque l'analyse de variance globale donnait des différences significatives. Nous avons ainsi comparé les résultats obtenus chez des animaux témoins dont le suc était recueilli soit par ligature soit par fistule et nous avons testé l'effet de l'huile d'olive par rapport aux animaux témoins respectifs. Il ressort de ce type de calcul que la sécrétion et l'irrigation des estomacs fistulés sont bien plus importantes que celles obtenues par ligature ($0{,}01 < p < 0{,}001$); ceci est valable pour tous les paramètres sécrétoires édudiés. Par ailleurs, lorsque l'on analyse l'effet de l'huile d'olive intraduodénale, on peut noter l'absence de résultats significatifs quand les animaux sont porteurs d'une ligature pylorique; mais si l'on examine l'effet de l'huile d'olive sur la sécrétion gastrique recueillie par fistule pylorique, on peut se rendre compte que le volume du suc, le débit d'acidité libre et le FSMG sont statistiquement diminués ($0{,}05 < p < 0{,}01$) par rapport aux animaux témoins également porteurs de fistule pylorique.

Discussion. Les résultats obtenus dans nos conditions indiquent donc un hyperfonctionnement de l'estomac fistulé par rapport à l'estomac ligaturé; il faut souligner que la période expérimentale est courte (90 min) mais nous l'avons délibérément choisie ainsi, pour que des facteurs de contróles secondaires et tardifs ne viennent pas masquer le phénomène que nous voulions étudier[22,23]. De toute manière nos préparations témoins ne sont pas stimulées par des agents exogènes, si ce n'est un «stress» au niveau du pylore. Or, si d'après BRODIE[2] la ligature pylorique provoque une hypersécrétion, il est par ailleurs classiquement admis que la présence d'acide dans la région antrale inhibe la libération de gastrine, ce qui ralentit secondairement la sécrétion; par contre, lorsqu'une fistule évacue le suc au fur et à mesure de sa formation, on peut penser que la gastrine exerce ses effets pendant une plus longue durée; cette hypothèse pourrait donc expliquer que le suc recueilli par fistule est quantitativement plus important, plus riche en acide et en pepsine; en même temps, un haut niveau de gastrine endogène maintiendrait le FSMG également à une valeur élevée[24].

La présence d'huile d'olive dans le duodénum d'animaux au pylore ligaturé ne provoque pratiquement pas de modifications significatives. Par contre, l'huile d'olive placée intraduodénalement chez des rats au pylore fistulé induit, dans nos conditions, une diminution significative de la sécrétion et de l'irrigation gastriques; si l'on considère que ce produit favorise la libération de CCK-PZ, on se trouve donc devant une intéraction hormonale et on peut alors penser que le CCK-PZ diminue la sécrétion gastrique entretenue, sinon stimulée, par la gastrine endogène. Nous retrouvons là un résultat analogue à celui de BROWN et MAGEE[25] qui ont montré chez le Chien que la CCK-PZ inhibe la stimulation acide provoquée par la libération endogène de gastrine au niveau d'une poche antrale irriguée par l'acétylcholine ou les peptones. Le mécanisme de cette inhibition serait de type compétitif, ces deux hormones partageant un récepteur commun au niveau de la cellule pariétale tout au moins chez le Chien[26]. Au niveau intestinal, le phénomène est sensiblement différent et il a été montré chez le Chat, que les hormones gastro-intestinales, élèvent le flux sanguin[27], probablement par la voie de neurones cholinergiques[28].

Quoi qu'il en soit, la stimulation gastrinique de la sécrétion gastrique est une phase normale du phénomène au cours de la digestion; aussi le recueil du suc gastrique par fistule, c'est-à-dire au cours d'une phase gastrinique de type digestif, nous paraît-il plus adéquat que l'usage de la ligature pylorique lorsque l'on veut étudier d'éventuelles actions ou interactions d'hormones gastro-intestinales.

Summary. Pylorus ligature hides the inhibitory effects of endogenous cholecystokinine-pancreozyme (CCK-PZ) on gastric mucosal secretion and irrigation, whereas the juice collected through transduodenal pyloric fistula makes this phenomenon obvious. It appears that the pyloric fistula encourages inhibition of gastrinic secretion, so that the CCK-PZ can achieve its effects.

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The Influence of Furosemide on the Renal Excretion of Chloramphenicol and its Metabolites

The renal excretion of chloramphenicol is usually at a relatively low rate, and its metabolites are apparently excreted only into urine[1,2]. A decrease in renal function results in accumulation of chloramphenicol metabolites in the organism[2]. The present work is an attempt to investigate whether this latter excretion can be influenced by a saluretic drug such as furosemide, not only to study the possibility of drug interaction but also because combinations of diuretic drugs and antibiotics such as chloramphenicol frequently have to be used in clinical practise.

In a group of 7 healthy, consenting volunteers, a single oral dose of 1 g chloramphenicol was given at 07.00 h and urine was collected by spontaneous voiding

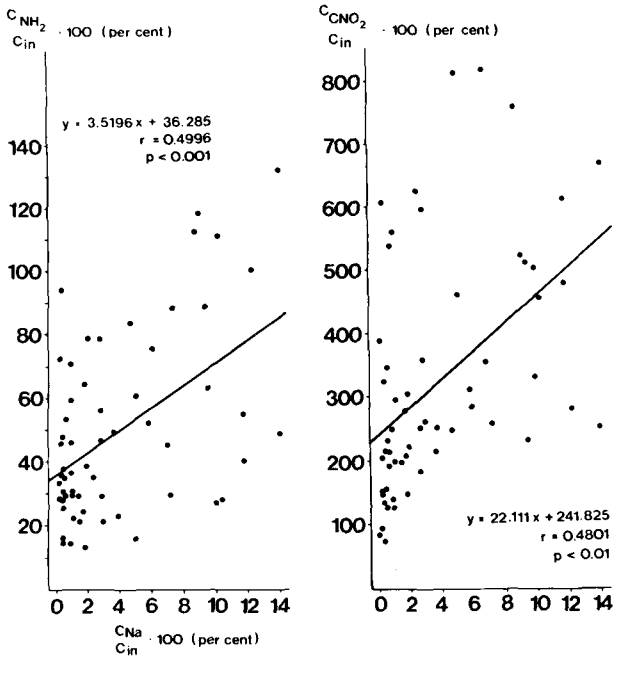
Urinary excretion of chloramphenicol (CH), arylamines (NH_2) and total nitrocompounds (CNO_2) after a single dose of chloramphenicol and after administration of chloramphenicol and furosemide.

Subject	Age	Sex	Chloramphenicol				Chloramphenicol + Furosemide			
			Urinary flow (ml/4 h)	Urinary excretion (mg/4 h)			Urinary flow (ml/4 h)	Urinary excretion (mg/4 h)		
				CH	NH_2	CNO_2		CH	NH_2	CNO_2
V.E.	51	♀	482	15.87	8.72	542.77	1021	10.76	13.66	1203.28
B.V.	28	♂	1170	15.30	12.42	380.12	1138	9.12	11.08	540.36
P.V.	49	♂	316	24.29	20.91	744.53	908	14.81	33.25	850.93
K.E.	49	♀	79	9.05	9.51	539.00	757	8.62	16.73	773.83
S.O.	49	♂	692	21.26	20.80	899.02	1795	12.72	31.02	964.32
N.V.	30	♂	591	21.66	9.18	657.84	1696	19.07	30.43	775.03
J.J.	48	♂	350	23.12	9.48	916.20	856	21.23	17.98	972.24
Average			525	18.75	13.00	668.49	1167	13.76	22.02	868.57
S.D.			347	5.58	5.50	198.4	412	4.89	9.24	207.24

at 4 one-hour intervals. The investigation was repeated on the same subjects 1 week later, but immediately after administration of the antibiotic, 10 mg of furosemide were injected i.v. In a further group of 9 patients with chronic renal disease, the same chloramphenicol dose was given orally at 06.00 h, and 10 mg furosemide injected at 09.00 h. Blood samples were taken from antecubital vein at 09.00, 10.30 and 12.00 h. Urine was collected by spontaneous voiding at 30-min intervals. In all cases, inulin was infused throughout at a rate of 0.36 ml/min.

In samples of serum and urine, chloramphenicol and its metabolites were measured by a method described elsewhere[3]. The results were expressed as chloramphenicol equivalents[1]. Inulin was estimated by the method of HARRISON[4] and Na concentrations were determined by routine photometry.

The Table gives the results in the healthy group. It is clear that furosemide, given just after antibiotic, resulted in a marked decrease in excretion of the latter ($p < 0.05$). The urinary excretion, however, of aryl amines and total nitro compounds significantly increased ($p < 0.05$). The Figure shows the results from the group of patients. The abscissa gives values of Na clearance (showing the effect of furosemide), the ordinate the clearance values of aryl amines and total nitro compounds. At thigher levels of Na excretion, the clearance of aryl amines approached that of inulin. The clearance of total nitro compounds was higher than that of inulin (in some cases by a factor of 6–8). This latter fact suggests significant tubular secretion of total nitro compounds.



Relationships between sodium clearance and renal clearances of aryl amines (C_{NH_2}) and total nitro compounds (C_{CNO_2}) calculated per 100 ml of inulin clearance (C_{in}), after administration of furosemide.

From previous observations, it would appear[5] that chloramphenicol is partially reabsorbed in the tubules after glomerular filtration of the diffusable fraction. There is the suggestion in the present work that furosemide influences tubular transport of the antibiotic. It is also possible that furosemide alters the binding of chloramphenicol to serum proteins, a factor which does not seem highly probable, but which must be excluded. The increase in clearance of aryl amines would appear to involve a decrease in tubular reabsorption. In some cases, with a high level of Na excretion, the clearance of aryl amines was higher than that of inulin, i.e. if reabsorption is completely supressed, tubular secretion can become manifest. The increase of total nitro compounds excretion over and above the clearance of inulin can be related to two possible mechanisms: increased tubular secretion or decreased reabsorption. The resultant clearance value clearly establishes that tubular secretion takes place, but is an arithmetic sum of two processes of opposite sign. Since in some cases the clearance of total nitro compounds was 8 × greater than the clearance of inulin (i.e. higher than usual values of filtration fraction – the ratio of glomerular filtration to plasma flow) it is also possible

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that the kidney is a site of formation of these metabolites. Questions as to whether the osmotic diuresis resulting from furosemide influences tubular transport of chloramphenicol metabolites by means of decreased water reabsorption, or whether Na ion has a specific effect, will require further study.

Summary. Simultaneous administration of chloramphenicol and furosemide (10 mg i.v.) decreased urinary excretion of chloramphenicol but increased the excretion of its metabolites as aryl amines and total nitro compounds. These latter increases were directly related to Na excretion.

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Dependence on Age of Methamphetamine-Produced Changes in Thermoregulation and Metabolism

It has been reported that the central stimulation which is one of the most prominent effects of amphetamines, diminishes with age[1–3]. The present experiments were performed in order to investigate whether this loss of effectiveness applies also to other actions of the amphetamines, i.e. the effect of methamphetamine on overall metabolism and thermoregulation.

Methods. Female NMRI mice aged 4–6 weeks (juvenile mice) or 20 months (old mice) were used. They were kept at 25 °C room temperature and fed ad libitum with standard diet (Herilan®) before and during the experiments. Methamphetamine (3 µg/g) was given s.c. immediately before the beginning of the experiments. Controls were treated with the same volume of saline. The animals were then placed singly into glass jars without bedding. Oxygen consumption was registered continuously by means of small spirometers, and the rectal temperature was measured at the end of the experiments as described earlier[4]. In another group of animals, 1 and 2 h after the drug administration blood glucose (according to HUGGETT and NIXON[5]), plasma non-esterified fatty acids (according to DUNCOMBE[6]) and liver glycogen (according to ESTLER and MITZNEGG[7]) were determined. For this purpose the animals were decapitated, liver samples were excised rapidly and frozen in liquid air within 10 sec. Blood was also collected from decapitated animals.

Results and discussion. As shown in the Table, juvenile mice react to methamphetamine with an increase of their oxygen consumption by almost 50 %. At the same time their body temperature rises significantly by 1.0 ± 0.3 °C over that of the control animals. These changes in overall metabolism are accompanied by a decrease of the glycogen content of the liver by ca. 60 % and a marked increase of the plasma non-esterified fatty acids. The blood glucose level remains nearly unchanged.

In contrast, in old animals liver glycogen declines only by 13 % while the blood glucose level drops by 31 mg/100 ml. Plasma non-esterified fatty acids increase even more than in the juvenile mice. For reasons discussed earlier[8], the oxygen consumption of old mice is lower than that of young animals, and it is only insignificantly raised by methamphetamine (Table). The rectal temperature of old mice treated with methamphetamine does not increase but falls significantly by 1.7 ± 0.5 °C.

These results suggest that juvenile mice treated with methamphetamine can easily mobilize their carbohydrate and lipid reserves and thus provide sufficient energy for thermogenesis and motor activity, which is increased considerably under these experimental conditions[2]. It is well known that in old animals the response of many

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Effect of methamphetamine (3 µg/g s.c.) on various metabolic parameters of old and juvenile mice

	Juvenile mice		Old mice	
	1st hour	2nd hour	1st hour	2nd hour
Oxygen consumption (Nml/g body weight/h)				
Controls (saline)	4.76 ± 0.29 (12)	4.41 ± 0.31 (12)	2.64 ± 0.20 (17)	2.43 ± 0.19 (15)
Methamphetamine	6.83 ± 0.73[a] (13)	6.51 ± 0.61[a] (14)	3.25 ± 0.37 (23)	2.75 ± 0.19 (20)
Liver glycogen (µmoles/g organ weight)				
Controls (untreated[b])	210 ± 8 (32)		206 ± 8 (32)	
Methamphetamine	82 ± 9[a] (22)	111 ± 12[a] (22)	168 ± 9[a] (22)	172 ± 8[a] (21)
Blood glucose (mg/100 ml)				
Controls (untreated)[b]	133 ± 3 (36)		134 ± 3 (36)	
Methamphetamine	135 ± 6 (23)	137 ± 5 (24)	107 ± 7[a] (23)	103 ± 7[a] (23)
Plasma non-esterified fatty acids (µeqiv/ml)				
Controls (untreated)[b]	0.49 ± 0.02 (36)		0.54 ± 0.03 (36)	
Methamphetamine	0.74 ± 0.03[a] (24)	0.71 ± 0.02[a] (24)	0.93 ± 0.03[a] (24)	0.87 ± 0.02[a] (24)

Mean values ± SEM are given, number of animals in parentheses. [a] Difference to control value significant, $p \leqslant 0.05$. [b] Untreated animals were used as controls because earlier studies have shown that injection procedure does not affect the parameters at the times given.