

liberated aromatic amine. The anaesthetic activities in Table 2 are expressed as the ratios of the molar concentrations of the compound studied (as the hydrochloride) and the standard giving the same anaesthetic effect. Each compound was tested for both superficial anaesthetic activity (rabbit cornea; cocaine as standard in conc.  $M/100$ ) and for infiltration anaesthesia (intra-dermal application to guinea-pigs; procaine as standard in conc.  $M/50$ ) so that its effectiveness might be judged on a broader basis. In the case of compounds "S 200" and "S 201", the first of these methods could not be used because of their low activity; the duration of complete anaesthesia of the cornea after applications of  $M/3$  solutions of these substances and of Xylocaine for comparison were therefore determined.

The results obtained so far show that both in compounds of the Xylocaine series and their carbamate analogues there is a distinct parallelism between the local anaesthetic effect and the resistance to hydrolysis with increasing *o*-methyl substitution. The only exceptions are the results with compounds "S 11" and "S 31" in infiltration anaesthesia; the difference between the two values (1.2 and 1.0), however, lies within the limit of error for the biological method of testing used.

Final conclusions as to the possible bearing of these results on the mechanism of action of the compounds studied must be postponed until the measurements of hydrolysis in alkaline solution and the determination of the activation energies and frequency factors now in progress have been completed. On the basis of these results it should then be possible to decide whether the effect noted is of steric or electronic origin.

We should like cordially to thank Dr. J. RUDINGER for the translation of this paper, which he has kindly made for us.

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#### Zusammenfassung

Die Reaktionsgeschwindigkeit der sauren Hydrolyse von Xylolain, Diethylaminoacet-*o*-toluidid und Diethylaminoacetanilid und seiner Carbat-Analoga wurde studiert: Die Stabilität dieser Verbindungen steigt mit fortschreitender Methyl-*o*-Substitution und verläuft mit ihren lokalanästhetischen Wirkungen parallel.

### Spontaneous Peristaltic Activity in Arteries and Veins of Adult Goldfinches and Albino Mice Cultivated *in vitro*

In previous studies, the occurrence of a spontaneous peristaltic activity was shown in embryonic arteries of chick (ATTARDI, GANDINI, and MARCON<sup>1</sup>; TONI<sup>2</sup>) and rabbit (ATTARDI<sup>3</sup>) and in veins of chick embryos and newly hatched chickens explanted *in vitro* (ATTARDI and ATTARDI GANDINI<sup>4</sup>).

<sup>1</sup> G. ATTARDI, E. GANDINI, and L. MARCON, Boll. Soc. ital. Biol. sper. 24, 1333 (1948).

<sup>2</sup> G. TONI, Boll. Soc. ital. Biol. sper. 29, 6 (1953).

<sup>3</sup> G. ATTARDI, Boll. Soc. ital. Biol. sper. 25, 1057 (1949).

<sup>4</sup> G. ATTARDI and D. ATTARDI GANDINI, Exper. 11, 37 (1955).

In this paper, evidence is presented that a similar contractile activity also occurs in arteries and veins of adult animals. For such investigations, animals of a small size, namely goldfinches (*Carduelis carduelis*) and albino mice (*Mus musculus*), were used, under the assumption that their vessels, owing to the small calibre and the thinness of the walls, should be in a suitable nutritive and mechanical condition for displaying a contractile activity in the plasmatic medium, into which they are explanted, as is the case with the embryonic vessels.

The isolated vessels were washed in physiological salt solution containing penicillin (50 units per cm<sup>3</sup>). Usually segments of vessel of 2 to 3 mm in length were explanted. The technique used was the same as described in the earlier reports; the culture medium was composed of chick plasma and ten day old chick embryo extract in equal parts.

The results of the experiments are shown in the Table.

In the adult goldfinch, all arteries tested, both central and peripheral, showed a contractile activity *in vitro*. The fact should be noted that this activity occurred in a very high percentage of explants (about 100%), in contrast to what was found in the case of embryonic arteries. Of the veins examined, a contractile activity was exhibited by those of the portal system and by the umbilical vein, a fact which had already been described in chick embryos and newly hatched chickens; moreover by some veins of the posterior portion of the body (coccygomesenteric vein, hypogastric vein, renal portal vein, femoral vein, external iliac vein, common iliac vein (anastomosis)<sup>1</sup>: in the latter veins a spontaneous contractility of a peristaltic type had also been observed in chick embryos in the last period of incubation and in newly hatched chickens (personal data not yet published).

The valve shaped as a perforated diaphragm which is situated where the common iliac vein empties into the efferent renal vein (SPANNER<sup>2</sup>) shows *in vitro* a rhythmic contractile activity, which is at present the object of a more detailed study.

In the arteries, the contractile activity is in most cases noticeably powerful and appears as typically coordinated. The contraction manifests itself as a contractile wave which almost always starts from one extremity of the explanted segment and propagates along the latter at a varying speed in the different explants, and is followed by a relaxation which likewise takes place successively in the following portions of the vessel. It is therefore justifiable to describe these contractions as of the peristaltic type, bearing in mind, of course, that their more or less typical character may be influenced by the particular conditions under which the explanted vessels are placed, on account of their isolation from the organism and of the lack of any internal pressure to keep their walls extended. The contractile activity starts immediately after explantation, or at least within the first hour, and generally becomes exhausted within 6-12 h; in several cases, however, persisting for longer periods, up to 2-3 days, although much weakened. The frequency of the contractions is generally higher in the more peripheral arteries. In the veins the contractile activity, which is likewise of a peristaltic type and fairly powerful, generally begins within the first hour and lasts from a few hours to 2 or 3 days.

<sup>1</sup> For the above indicated veins the terminology proposed by R. SPANNER, Morph. Jb. 54, 560 (1925), has been used.

<sup>2</sup> R. SPANNER, Morph. Jb. 54, 560 (1925).

Goldfinch		Albino mouse	
Vessel	Frequency of the contractions at 38,5° C (min. and max. values)	Vessel	Frequency of the contractions at 38,5° C (min. and max. values)
Common carotid artery . . . . .	5–13	Brachial artery . . . . .	4–11
Brachial artery . . . . .	24–42	Median artery . . . . .	13–28
Interosseous artery of the wing . . . . .	24–29	Intercostal artery . . . . .	14–65
Superficial ulnar artery . . . . .	28–66	Hepatic artery . . . . .	6–13
Thoracic aorta . . . . .	5	Left gastric artery . . . . .	4
Abdominal aorta . . . . .	15–27	Lienal artery . . . . .	4–25
Coeliac artery . . . . .	16–49	Superior mesenteric artery . . . . .	3–24
Right hepatic artery . . . . .	14–90	Internal spermatic artery . . . . .	4–19
Left hepatic artery . . . . .	26–103	Renal artery . . . . .	18–32
Superior mesenteric artery . . . . .	14	Inferior mesenteric artery . . . . .	4–17
Superior renal artery . . . . .	25	External iliac artery . . . . .	5– 7
Femoral artery . . . . .	18–53	Femoral artery . . . . .	4–27
Internal pelvic artery . . . . .	11–35	Saphenous artery . . . . .	5–11
Sciatic artery . . . . .	20	Anterior tibial artery . . . . .	8–17
Anterior tibial artery . . . . .	13–45	Caudal artery . . . . .	8–18
Common pudendal artery . . . . .	10		
Middle coccygeal artery . . . . .	11–14		
Right portal vein . . . . .	19–67	Portal vein . . . . .	48–72
Common mesenteric vein . . . . .	59	Lienal vein . . . . .	20–24
Left portal vein . . . . .	3–16	Internal spermatic vein . . . . .	6–23
Umbilical vein . . . . .	8–14		
Coccygomesenteric vein . . . . .	7–25		
Hypogastric vein . . . . .	9–13		
Renal portal vein . . . . .	2–12		
External iliac vein . . . . .	6–22		
Femoral vein . . . . .	17–31		
Common iliac vein ("Anastomosis") . . . . .	6–23		

In the adult mouse, the central and peripheral arteries have also exhibited *in vitro* a rhythmical contractile activity; here too, in a high percentage of explants (about 60%). In some cases the contractions are very powerful and clearly peristaltic, in other cases only by middle power observation can the rhythmical oscillations of the walls be seen. The contractions start within the first hour of incubation and last for 1 or 2 h, more often however for longer, up to 2–3 days; in other cases, the contractile activity manifests or reaches its maximum only on the 2nd or 3rd day.

Of the veins of the adult mouse tested, a rhythmical contractile activity was observed in the portal, lienal and internal spermatic veins. In the portal vein, the activity is strikingly powerful and with a very high frequency of the contractions. It can often be noticed before transferring the fragment to the plasma, while it is still in the salt solution under the dissecting microscope. The contractions, which are of a peristaltic type, last *in vitro* for a long time (up to more than 15 days without washing or renewal of the culture medium), decreasing gradually in frequency but conserving a considerable energy. In the lienal and internal spermatic veins, the rhythmical activity observed was generally slight: it started immediately after the explantation and lasted only for a very short time (from a few minutes to half an hour), probably in connection with the occurrence of a progressive and quick retraction of their walls, which could be recognized from the narrowing of the lumen. Such a rapid and considerable retraction of the walls was noticed in a great part of the other veins tested, and the negative findings obtained on such vessels may perhaps be due precisely to this fact, rather than to the absence of a spontaneous contractility.

The results reported above provide the first direct evidence, since the discovery of the pulsatile veins of the bat wings (WHARTON JONES<sup>1</sup>, HESS<sup>2</sup>, MISLIN<sup>3</sup>), of the occurrence of a rhythmical peristaltic activity in the arteries and veins of adult birds and mammals: on account of the high intensity and frequency of the contractions, which are possibly still higher *in vivo*, it seems a reasonable supposition that this rhythmical activity plays a significant role in the mechanism of the circulation.

Further work on this subject is now in progress.

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Résumé

L'auteur a mis en évidence une activité contractile spontanée et rythmique de type péristaltique dans les artères centrales et périphériques et dans quelques veines du système porte et de la moitié postérieure du corps, cultivées «in vitro». Les observations ont été faites sur un Oiseau (*Carduelis carduelis*) et un Mammifère (*Mus musculus*).

<sup>1</sup> T. WHARTON JONES, Philos. trans. roy. Soc. London, 1852.  
<sup>2</sup> W. R. HESS, Pflügers Arch. 173, 243 (1919).  
<sup>3</sup> H. MISLIN, Helv. physiol. Acta [C] 5, 3–4 (1947).