RESPONSIVENESS OF ISOLATED DOG VEINS TO BRADYKININ:
DISTRIBUTION AND A POSSIBLE CORRELATION WITH
GENESIS OF THE VENOUS SYSTEM

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Although it has become clear that the venous system is pharmacologically unhomo-
genous, the information is still fragmentary (1, 2).

The veins studied in this experiment were cephalic, external jugular, azygos, pulmo-
nary, hepatic, portal, splenic, renal, femoral and lateral saphenous veins as well as anterior
vena cava and three divisions of posterior vena cava (proximal to the diaphragm, between
the liver and the renal veins, and distal to the renal veins), fourteen in all.

Segments of these veins were obtained from 20 male mongrel dogs of 9 to 21 kg body
weight, under pentobarbital anesthesia. Helical strips (30 to 40 mm long, 2 mm wide)
were cut from these segments, and suspended in a 10 ml organ bath under a resting tension
of 0.2 to 0.4 g. Only the portal vein was made to form a longitudinal strip. The bath
contained Krebs-bicarbonate solution aerated with 95% O2-5% CO2 and was maintained
at 37°C. Isotonic contractions were recorded on smoked drums. In the division of
the posterior vena cava between the liver and renal veins, however, the net contraction was
too small to be recorded isotonically. Therefore, an electric transducer (Kyowa-Dengyo,
120T-10B) was used to record the tension development isometrically on an ink-writing
oscillograph.

The agents used were norepinephrine (1-Arterenol bitartrate, Sigma; NE) and brady-
kinin (Protein Research Foundation, Osaka; BK). Dose-response curves (D-R curves)
were obtained in a cumulative manner.

In preliminary experiments, several vasoactive substances such as NE, ACh, histamine,
5-HT, angiotensin II and BK were tested. Among these agents, NE induced the largest
contraction in almost all preparations obtained from various sites of the venous system.
Therefore, the contraction produced by NE was taken as standard, the effects of BK were
compared and the results are summarized in Fig. 1.

The average D-R curve for NE is indicated by the thick line. This curve was com-
puted from the D-R curves for NE of 14 different veins studied (3 to 5 animals were used
to obtain each D-R curve). The ED50 values of veins for NE ranged from $1.0 \times 10^{-7}$ M
(portal vein) to $1.3 \times 10^{-9}$ M (posterior vena cava between the liver and the renal veins).

1 These results were presented at the 14th General Meeting of Japanese College of Angiology,
The degree of contraction produced by BK is expressed as the percent of the maximum contraction obtained by NE in the same preparation. Each point represents the mean of 3 to 5 measurements (3 to 5 animals).

Dose-dependent contractions were clearly observed in pulmonary, hepatic, portal, and splenic veins, anterior vena cava, and two divisions of posterior vena cava (proximal to the diaphragm and between the liver and the renal veins) (21-7 in Fig. 1). The response to BK exceeded that to NE only in the supradiaphragm division of posterior vena cava. The response of cephalic, external jugular, azygos, femoral, and lateral saphenous veins and posterior vena cava (distal to the renal veins) was very low. Maximum contractions induced by 10^{-5} M BK were less than 5% of that by NE (29-14 in Fig. 1). Renal veins showed individually different responses.

On the basis of these results, the veins can be classified into two groups, as schematically shown in Fig. 2: one group includes veins highly sensitive to BK such as those in the visceral area (21-7), and the other group those veins which have a low sensitivity to BK such as those in extremities and the body wall (29-14). Renal veins (28) appear to be of an intermediate nature.
A striking parallel is noted between the distribution of the two groups of veins and the genesis of the venous system. Textbooks of Embryology (3, 4) state that most veins of the extremities and the body wall originate from the cardinal vein system, i.e., the anterior and posterior cardinal veins as well as the subcardinal and supracardinal veins. It was clarified in the present experiment that the distribution of the veins with a low sensitivity to BK (black portions in Fig. 2) coincides, as a whole, with that of veins that originate from the cardinal vein system. It is also known that the three divisions of the posterior...
vena cava develop from distinct parts of the embryonal venous tree and that only the division distal to the renal veins (212 in Fig. 2) originates from the cardinal vein system. The latter part of the posterior vena cava proved to be insensitive to BK, whereas the proximal divisions (21 and 2 in Fig. 2) responded remarkably (Fig. 1). There is, however, one important exception: the anterior vena cava proved to be very sensitive to BK (24 in Fig. 1) though it originates from the right anterior cardinal vein.

Although these studies are still in progress, the results herein indicate that there is a close relationship between the genesis of the venous system and regional differences in sensitivity to BK.

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REFERENCES

EFFECT OF DIBUTYRYL ADENOSINE 3', 5'-MONOPHOSPHATE ON CATECHOLAMINE SYNTHESIS IN RAT BRAIN CORTICAL SLICES AND ISOLATED VASA DEFERENTIA

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Results of recent studies indicate that cyclic adenosine 3', 5'-monophosphate (cAMP) regulates catecholamine synthesis, and the evidence is as follows. a) Administration of dibutyryl adenosine 3', 5'-monophosphate (DB-cAMP) to hypophysectomized rats restored the activities of both tyrosine hydroxylase (TH) and dopamine-3-hydroxylase (DBH) in the adrenal gland (1). b) Prolonged culture of mouse neuroblastoma tissue with DB-cAMP increased the activity of TH (2). c) Incubation of isolated rat superior cervical ganglia with DB-cAMP increased the levels of both DBH and noradrenaline (NA) (3). d) Injection of carbamylcholine, reserpine or amphetamine increased the cAMP content of rat adrenal medulla, which might cause increase in the medullary TH activity (4). Recently, Goldstein et al. reported that DB-cAMP stimulated the synthesis of 14C-DA from 14C-tyrosine in striatal slices (5). In addition, the present authors recently found that DB-cAMP increased 14C-catecholamine (CA) synthesis from 14C-tyrosine in adrenal medullary slices several-fold, mainly through its effect on TH (in preparation).