spleen, femur and intestine, the determinations being made at 180 min following the delivery of ^{59}Fe. In the case of intestine the ^{59}Fe uptake was determined immediately after removal as well as following washing the lumen with a known volume of saline or after dessication during 24 h at 80 °C. The dry and wet weights of intestine and the wet weights of spleen and liver were also obtained and results refered to cpm of ^{59}Fe per 100 mg of organ. Counts in blood and femur were expressed per 100 g b.wt and per femur, respectively. For statistical assessment the results were compared employing Student's t-test and differences between means were considered significant if $p=0.05$ or less.

Results. The table shows that at 180 min following the administration of ^{59}Fe accompanied by ASA there is a significant increase of counts, in comparison with the untreated controls, in blood, spleen, liver and femur. On the other hand, in freshly removed, in wet washed or in dry intestine of the ASA treated group the values were comparable to those found in controls.

Discussion. The foregoing results suggest that in the rat the action of ASA is to augment the absorption of iron. This influence is evident at 3 h following ingestion through a catheter placed in the stomach. Indeed an enhanced count of ^{59}Fe in the ASA-treated group was found in blood, spleen, liver and femur, whereas comparable iron counts were detected in the freshly removed, the wet washed as well as in the dry intestine. It is therefore plausible that an enhanced intestinal iron absorption in the ASA-treated group is followed by higher circulating levels of iron and by an enhancement in deposit organs. The influence of ASA on this phenomenon could probably be related to the action of ASA on the intestinal cycloxygenase system. However it must be noticed that another effect of the drug, independent of the mechanism of prostaglandin inhibition (e.g. purely chemical mechanisms such as are already known with ascorbic acid) cannot be discarded. Nevertheless the tentative hypothesis regarding the participation of prostaglandins is plausible in view of in vitro studies documenting that these compounds can alter iron fluxes through the intestine. Indeed, the present results are compatible with previous findings indicating that prostaglandins E_1 and E_2 diminished the passage of iron across the mucosa and serosa of the isolated rat intestine as well as with the report that indomethacin is able to enhance the same process in vitro[14].

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3 J.J.M. Marx, Blood *53*, 204 (1979).
4 F.A. El-Shobaki and W. Rummel, Res. exp. Med. *171*, 243 (1977).
5 M. Layrisse, J.D. Cook, C. Martinez, M. Roche, I.N. Kuhn, R.B. Walker and C.A. Finch, Blood *33*, 430 (1969).
6 C. Martínez Torres and M. Layrisse, Wld Rev. Nutr. Diet. *19*, 51 (1974).
7 G. Pirzio Biroli, T.H. Bothwel and C.A. Finch, J. Lab. clin. Med. *51*, 32 (1958).
8 F. El-Shobaki and W. Rummel, Res. exp. Med. *173*, 119 (1978).
9 R.W. Charlton, P. Jacobs, J.D. Torrance and T.H. Bothwell, J. clin. Invest. *44*, 543 (1965).
10 W.H. Crosby, Blood *22*, 441 (1963).
11 M.E. Conrad and W.H. Crosby, Blood *22*, 406 (1963).
12 G. Pirzio Biroli and C.A. Finch, J. Lab. clin. Med. *55*, 216 (1960).
13 G. Mendel, Blood *18*, 727 (1961).
14 A. Gutnisky, E. Speziale, P. Glikman, M.F. Gimeno and A.L. Gimeno, Acta physiol. latinoam. *30*, 217 (1980).

Comparison of the responsiveness of isolated arteries and veins taken from the same dogs 17 days apart

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Summary. The present experiments demonstrate that isolated arteries and veins taken from the same dogs before and after an interval of 17 days show comparable responses to adrenergic nerve stimulation, exogenous norepinephrine and depolarizing solution. They provide an acceptable model for the in vitro study of chronic influences on canine vascular responsiveness.

The aim of the present experiments was to determine whether or not 2 sets of isolated blood vessels can be obtained from the same dogs after a sufficient time interval to allow the study of the effects of chronic surgical interventions or chronic administration of drugs on vascular responsiveness.

Pairs of dogs (mean weight 25.1 ± 2.4 kg) from the same litters ($n=6$) were studied on the same days. On day 1, the dogs were anesthetized with pentobarbital (30 mg/kg, i.v.); segments (3 cm) of the lateral saphenous vein and of the tibial artery of the left hindpaw were removed. After surgery, the dogs were allowed to recover. On day 17, the dogs were anesthetized again with pentobarbital; the lateral saphenous vein and the tibial artery of the right hindpaw were then removed.

From each segment of saphenous vein and tibial artery, 3 rings (4 mm width) were prepared and these were mounted in organ chambers filled with aerated Krebs-Ringer solution at 37 °C (m molar composition: KH_2PO_4, 1.2; NaCl, 118.3; KCl, 4.7; $MgSO_4$, 1.2; $CaCl_2$, 2.5; $NaHCO_3$, 25; Na_2Ca EDTA, 0.026; glucose, 11.1). The preparations were placed at the optimal point of their length-tension curve using a standard electrical stimulation[1,2]. After 30 min equilibration, either a frequency-response curve to electrical stimulation[3], a dose-response curve to norepinephrine, or a dose-response curve to increasing concentrations of K^+ in the presence of 10^{-5} M phentolamine[4,5], were obtained simultaneously in the 3 segments from each saphenous vein and tibial artery. For statistical analysis, Student's t-test for unpaired observations was used. The responses of both blood vessels of the same dog were compared on day 1 and day 17, while the comparison between the 2 dogs of the same litter was performed either on day 1 or day 17.

The optimal tension was comparable in the 4 groups of arteries and in the 4 groups of saphenous veins. In both the arteries and the veins similar frequency-response curves to electrical stimulation (0.5-64 Hz) were obtained on day 1 and day 17; no significant differences were noted between

Responsiveness to electrical stimulation and K^+ in presence of phentolamine (10^{-5} M) in canine veins and arteries*

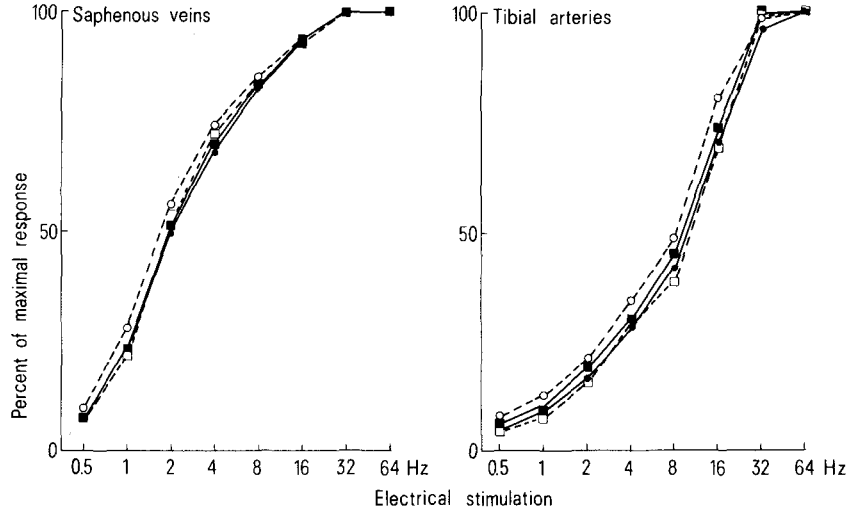
Norepinephrine

Concentration (M)	Saphenous veins Dogs 1 Day 1	Saphenous veins Dogs 1 Day 17	Saphenous veins Dogs 2 Day 1	Saphenous veins Dogs 2 Day 17	Tibial arteries Dogs 1 Day 1	Tibial arteries Dogs 1 Day 17	Tibial arteries Dogs 2 Day 1	Tibial arteries Dogs 2 Day 17
10^{-8}	0.72±0.27	1.23±0.80	0.76±0.30	0.38±0.25	0	0	0	0
3×10^{-8}	2.75±0.97	5.05±1.63	3.24±1.19	3.23±1.47	0	0	0.10±0.10	0.14± 0.14
10^{-7}	10.9 ±2.6	17.1 ±3.6	13.8 ±3.8	12.6 ±2.6	0.31±0.20	0.81± 0.59	1.25±1.04	0.75± 0.55
3×10^{-7}	27.9 ±4.4	31.7 ±4.8	28.7 ±4.7	34.0 ±4.9	1.76±0.48	3.30± 1.15	2.43±1.50	6.57± 5.74
10^{-6}	46.9 ±4.8	51.3 ±5.8	49.8 ±4.7	53.7 ±5.7	12.6 ±1.6	13.7 ± 5.0	8.47±3.36	17.4 ± 8.5
3×10^{-6}	67.7 ±5.1	68.7 ±5.1	67.3 ±4.1	72.1 ±6.1	20.6 ±3.1	28.6 ± 9.4	20.7 ±7.9	30.7 ±10.2
10^{-5}	86.8 ±4.1	88.8 ±3.5	84.5 ±3.7	87.4 ±5.0	50.7 ±7.3	64.4 ±10.1	55.7 ±9.3	55.1 ± 9.9
3×10^{-5}	97.4 ±1.8	97.3 ±2.7	94.4 ±2.0	94.8 ±3.2	87.6 ±4.6	89.2 ± 5.4	92.9 ±3.3	87.5 ± 4.1
10^{-4}	99.5 ±0.5	100	100	98.0 ±1.5	99.8 ±0.2	97.3 ± 2.2	99.2 ±0.8	97.2 ± 1.9
3×10^{-4}	100	100	100	100	100	100	100	100

K^+ in presence of phentolamine (10^{-5} M)

K^+ (mM)	Saphenous veins Dogs 1 Day 1	Saphenous veins Dogs 1 Day 17	Saphenous veins Dogs 2 Day 1	Saphenous veins Dogs 2 Day 17	Tibial arteries Dogs 1 Day 1	Tibial arteries Dogs 1 Day 17	Tibial arteries Dogs 2 Day 1	Tibial arteries Dogs 2 Day 17
30	50.1±3.8	48.9±4.4	53.3±7.4	44.1±8.3	26.4±12.7	19.4± 7.9	37.2±8.5	30.0±12.5
40	69.1±2.4	74.4±4.3	72.1±4.4	70.7±6.2	78.7± 7.1	81.2± 9.6	86.7±7.2	73.3± 4.8
50	85.7±2.5	89.4±3.1	88.7±3.6	83.2±5.2	89.6± 1.8	103.3±16.8	93.5±3.0	88.8± 5.3
60	95.7±1.7	97.2±1.1	95.3±2.9	95.1±2.0	99.0± 0.7	110.2±10.7	98.5±1.0	101.7± 0.8
70	100	100	100	100	100	100	100	100

* Results expressed as percent of maximal responses and shown as means ± SEM for 6 dogs in each group; 2 groups (dogs 1 and dogs 2) from the same litters are compared.



Effect of activation of the adrenergic nerve endings by electrical stimulation at increasing frequencies in saphenous veins (left) and tibial arteries (right) from dogs taken from the same litter (○, □, respectively) and studied on day 1 (full symbols, full lines) and day 17 (open symbols, broken lines). Data shown as means for 6 dogs in each group; for the sake of clarity the SEM are omitted. No statistically significant differences were observed between the different groups.

dogs of the same litter; the maximal responses to the electric impulses were comparable in the four groups of either arteries or veins (fig.). A similar absence of difference in responsiveness between arteries and veins taken on day 1 and day 17, or between blood vessels from dogs taken from the same litter was noted when the preparations were made to contract with norepinephrine (10^{-8} to 3×10^{-4} M) or K^+ (30–70 mM) (table).

The present experiments thus demonstrate that at intervals of up to 2 weeks the responsiveness of isolated canine arteries and veins to electrical stimulation of the adrenergic nerve endings[3,6,7], to alpha-adrenergic activation[2,8,9] and to depolarizing solution[4,5] is unchanged. They also demonstrate that blood vessels of 2 dogs from the same litter, studied in parallel, exhibit comparable responsiveness to those stimuli. The present investigation thus provides an acceptable model for the study of the effects of chronic surgical procedures or prolonged administration of drugs on the adrenergic neuroeffector interaction and smooth muscle responsiveness in the canine blood vessel wall, whereby each dog can serve as its own control, and dogs with the same genetic background can serve as time controls.

1 P. Vanhoutte and I. Leusen, Pflügers Arch. *306*, 341 (1969).
2 J. De Mey and P.M. Vanhoutte, Blood Vessels *17*, 27 (1980).
3 P. Vanhoutte, D. Clement and I. Leusen, Archs int. Pharmacodyn. *167*, 495 (1967).
4 P.M. Vanhoutte and T.J. Verbeuren, Circulation Res. *39*, 263 (1976).
5 N.J. Rusch, J.T. Shepherd and P.M. Vanhoutte, J. Physiol. *311*, 57 (1981).
6 P.M. Vanhoutte, R.R. Lorenz and G.M. Tyce, J. Pharmac. exp. Ther. *185*, 386 (1973).
7 P.M. Vanhoutte, E.P. Coen, W.J. De Ridder and T.J. Verbeuren, Circulation Res. *45*, 608 (1979).
8 P.M. Vanhoutte and J.T. Shepherd, Circulation Res. *32*, 259 (1973).
9 J. De Mey and P.M. Vanhoutte, Circulation Res. *46*, 826 (1980).