the thromboplastic and fibrinolytic activities of the various tissues of the eye (human and pig). High thromboplastic activity was found in retina and choroid, while sclera, cornea, lens and vitreous body were only slightly active. High fibrinolytic activity was observed in choroid while retina had medium or low activity. Sclera was low in fibrinolytic activity and cornea, lens and vitreous body were inactive or nearly inactive. The results suggest a connection between the hemostatic balance in the various tissues and some pathological processes in the eye.

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Oxygen Content and pH of Arterial, Venous and Portal Blood in Dogs After Histamine. (27137)

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Vascular reaction to histamine(1-5) is characterized by capillary hypotonia, change of hydrostatic pressure, increased permeability, arteriolar dilatation and venous constriction. This syndrome may become irreversible in histaminic shock(6). Engorgement of the liver and splanchnic viscera, in dogs given histamine, increased with constriction of hepatic veins(7), may result in stagnant anoxia and damage of gastrointestinal tract.

The purpose of the present work was to study the changes in oxygen content and pH of blood drawn from the femoral artery, femoral and portal veins in dogs after histamine to determine whether stagnant anoxia of splanchnic area occurs after histamine.

Methods. Mongrel male dogs 20 to 24 kg under sodium pentobarbital anaesthesia (30 mg/kg B.W.) and heparinized with 3 mg/kg had the femoral artery and vein cannulated with polyethylene tubes. After subcostal laparotomy the portal vein was cannulated inferior to the junction of superior pancreaticoduodenal vein. After cannulation, pre-treatment samples of blood were drawn.

Histamine dihydrochloride (Roche) was injected intramuscularly (5 mg/kg)(5), immediately after first sampling. Despite the short period of tachypnea and hypotension,

TABLE I. Blood O_2 Content (ml O_2/100 ml Blood) before (0) and after Injection of Histamine* (10, 20, 30 Min.).

	6 histamine treated dogs			4 controls, no treatment		
Time, min.	A	V	P	A	V	P
0	21.48 18.04–23.41	11.01 9.62–12.37	13.21 11.11–13.62	22.95 20.86–25.74	13.55 9.34–17.32	16.00 12.47–20.93
10	20.06 16.54–22.69	9.21 5.02–11.38	12.41 10.79–13.00	22.60 20.55–25.10	13.31 8.69–17.10	16.20 12.67–21.10
20	18.38 15.58–19.55	7.92 3.50–11.30	10.02 7.83–12.31	22.40 20.55–25.14	13.30 8.84–17.10	15.68 12.43–21.00
30	17.19 12.05–18.35	6.71 1.99–10.62	8.88 4.08–11.14	22.95 20.55–25.57	13.00 8.69–17.00	15.31 12.43–20.80

* Histamine dihydrochloride, 5 mg/kg B.W.
A = Femoral artery. V = Femoral vein. P = Portal vein. Avg values and range.

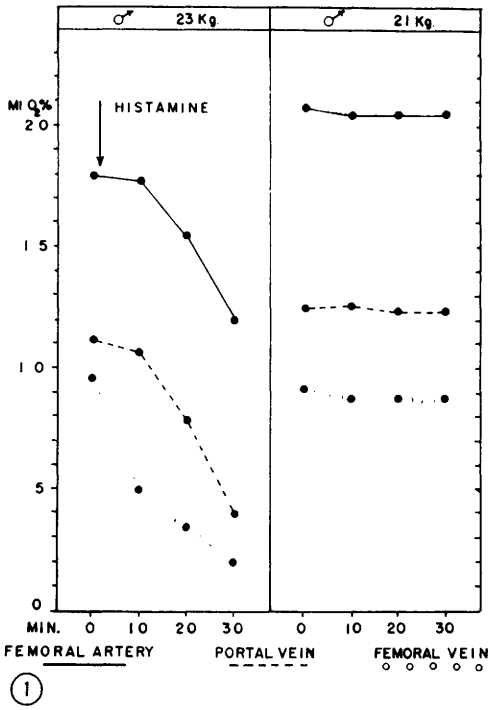

FIG. 1. Typical curves of posthistaminic changes of blood O_2, in a dog, compared with an untreated control.

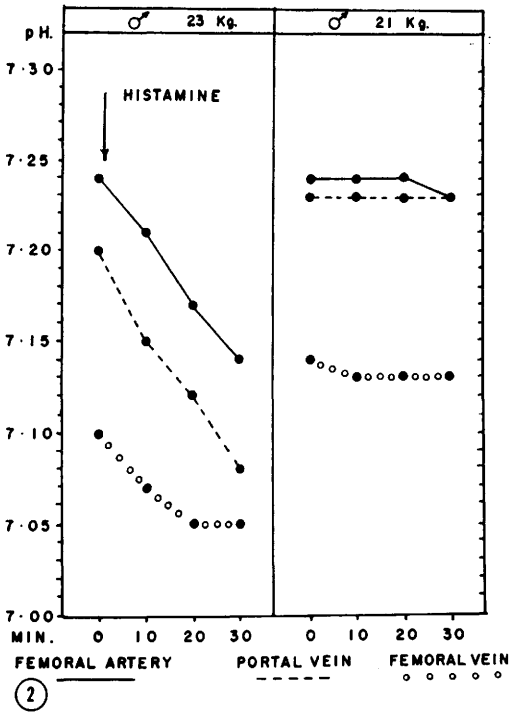

FIG. 2. Typical curves of posthistaminic changes of blood pH, in a dog, compared with an untreated control.

this dose is tolerated by dogs. Three further samples of blood from cannulated vessels were taken 10, 20 and 30 minutes after injection of histamine. A group of control dogs received no histamine, but surgery and sampling in these dogs was the same as in the treated animals. Blood was analyzed immediately after collection for pH and oxygen content. Determination of oxygen in whole blood was performed by the Van Slyke manometric method.

Results. Oxygen content and pH of blood was decreased in all dogs injected with histamine, as compared with untreated controls (Tables I and II). Example of a marked reaction to histamine in a dog, compared with an untreated control, is given in Fig. 1 and 2 which show the curves of changes of O_2 and pH respectively.

Comment. Simultaneous determination of

TABLE II. Blood pH before (0) and after Injection of Histamine* (10, 20, 30 Min.).

	6 histamine treated dogs			4 controls, no treatment		
Time, min.	A	V	P	A	V	P
0	7.25 7.24–7.28	7.12 7.10–7.18	7.21 7.14–7.26	7.27 7.23–7.28	7.19 7.14–7.22	7.24 7.20–7.26
10	7.20 7.16–7.24	7.10 7.08–7.18	7.12 7.09–7.20	7.27 7.23–7.28	7.18 7.13–7.22	7.24 7.20–7.26
20	7.18 7.15–7.24	7.08 7.05–7.12	7.12 7.06–7.19	7.27 7.23–7.29	7.18 7.13–7.22	7.23 7.20–7.26
30	7.15 7.12–7.22	7.06 7.04–7.11	7.09 7.04–7.17	7.27 7.23–7.29	7.17 7.13–7.21	7.23 7.19–7.26

* Histamine dihydrochloride, 5 mg/kg B.W.

A = Femoral artery. V = Femoral vein. P = Portal vein. Avg values and range.

total blood O_2 and pH in femoral artery and vein and portal vein show marked parallelism of the response to histamine. Decrease of O_2 and pH after injection of histamine resembles stagnant anoxia due to other causes such as shock.

Injury to capillaries and to parenchymatous tissues of the area of portal circulation by hypoxia(8,9) may occur in histamine treated animals. Such injury associated with acid and peptic hypersecretion may contribute to the etiology of acute and chronic posthistaminic gastric lesions(2,3,4,5).

Summary. Blood from femoral artery and vein and from portal vein of dogs was sampled before and 10, 20 and 30 minutes after injection of histamine. Oxygen content and pH of the blood was determined. Marked decrease of both O_2 and pH of blood was found in all histamine treated animals as compared with untreated controls. The pattern of this reaction corresponds to one observed in stagnant anoxia and acidosis. Stagnant anoxia of splanchnic area which occurs after histamine is considered an important etiological factor responsible for the posthistaminic gastric lesions.

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An Orally Effective Mammalian Antifertility Agent. (27138)

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Reproduction of the species represents a culmination of many intricate mechanisms, each potentially susceptible to modification by chemical agents. Of the numerous biological contraceptives available, relatively few can be considered practical for control of mammalian reproduction(1,2,3). This paper pertains to biological spectrum of U-11555A,* one member of a new series of 2,3-diphenylindenes, which on the basis of the following data is considered to be a potent, orally effective antifertility agent in laboratory mammals. Chemistry of these compounds has been reported elsewhere(4).

Methods and results. Sprague-Dawley rats, fed Purina Laboratory Chow *ad libitum* and maintained in an environment of 78 ± 2°F, were used.

Pregnancy inhibition. Proestrus 200 g rats were placed with males of proven fertility. The day sperm were identified in vaginal smear was considered Day 1 of pregnancy. On Day 8 females were sacrificed and uteri examined for implantation sites and gross abnormalities. Administration of U-11555A† from proestrus to Day 6, at 0.5 mg/kg/day and above, was 100% effective in inhibiting pregnancy (Table I). A single dose of 2.5 mg/kg, administered within 4 days post insemination, was equally effective in preventing pregnancy, whereas single doses up to 25 mg/kg, administered on Day 5, were ineffective in inhibiting pregnancy (Table II). Five females received 2.50 mg/kg/day from Day 5 through Day 8; at autopsy on

* Triethylamine, 2-(*p*-[6-methoxy-2-(*p*-methoxyphenyl)-inden-3-yl]-phenoxy) hydrochloride.

† In all experiments U-11555A was administered orally in Upjohn Sterile Vehicle No. 122, containing 0.25% methylcellulose.