which could truly be termed a classical Arthus Phenomenon or local anaphylaxis. Precipitin antibodies were also measured in the blood serum in an endeavor to determine whether the material, as in the case of necrosin, proved to be antigenic. In no instance was there any appreciable level of antibody found in the serum. The readings in the serological tubes were completely negative, or at most with high concentration of the antigen (*i.e.* the LPF) a mere trace of cloudiness could at times be discerned. The facts indicated that the leukocytosis-promoting factor obtained from canine exudates was essentially non-antigenic to the rabbit.

Subsequently, observations were made on guinea pigs with the leukocytosis-promoting factor of dog exudates in an attempt to determine whether the active material is capable of inducing a state of anaphylaxis. The leukocytosis-promoting factor contained in 1 cc of aqueous fluid was injected subcutaneously in several guinea pigs. About a month later a similar dose of the active material was reinjected intraperitoneally. In no case was there any evidence of the least sign of discomfort to respiration or any other anaphylactic manifestations. These observations corroborated further the evidence obtained in rabbits that the factor from exudates of another species is essentially non-antigenic. Furthermore, when the leukocytosis-promoting factor of human exudates was injected into a dog at varying intervals of about a month apart or thereabouts, there was no appreciable evidence found of any anaphylactic reaction following such injections.

Conclusions. The indications are that the leukocytosis-promoting factor of inflammatory exudates is essentially non-antigenic, *i.e.* when the active material derived from one animal form is introduced into an animal of a completely different species. The present observations should serve to dispel, in large part, any apprehension that may arise in regard to the possible clinical application of the leukocytosis-promoting factor.

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Upper Auriculo-Ventricular Rhythm (Coronary Sinus Rhythm) Experimentally Produced.*

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If an a-v rhythm presents inverted P-waves preceding the QRS-complex at a normal or slightly shortened distance, the focus of origin is supposed to be situated in that part of the a-v node which extends to the coronary sinus. This assumption is based on experiments of Zahn[1] who warmed this area by means of a thermode, and studies by Meek and Eyster[2] who used direct leads in order to locate the area of primary activity. Zahn did not record electrocardiograms, and some doubt was expressed to the effect that it is not possible to warm such a small focus (Meek and Eyster)[1] and that the determination of the precise site of stimulus formation in such small structures with the methods employed is "precarious" (Lewis).[3]

Therefore, it seemed desirable to obtain further evidence that stimulus formation takes place in the coronary sinus if the electrocardiogram described above is registered.

In a previous study it was demonstrated[4] that in hearts of dogs, perfused by the Langendorff method, warming of the coronary

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1 Zahn, A., *Arch. f. Physiol.*, 1913, **151**, 247.

2 Meek, W. J., and Eyster, S. A. E., *Heart*, 1914, **5**, 227.

3 Lewis, Th., *The Mechanism and the Graphic Registration of the Heart Beat*, 3rd ed., 1925.

4 Scherf, D., *Z. ges. exp. Med.*, 1931, **78**, 511.

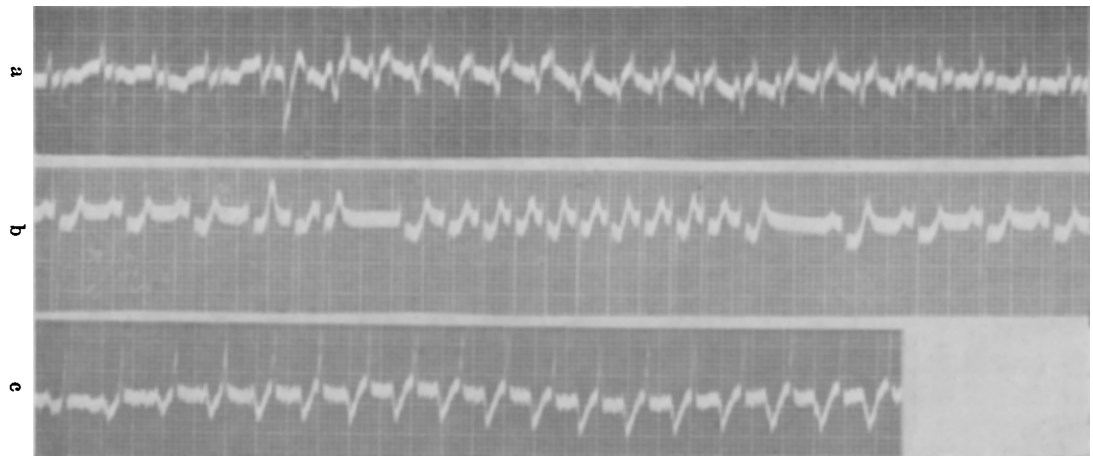

FIG. 1a.
Warming of the coronary sinus area through the wall of the coronary sinus vein causes coronary sinus rhythm with inverted P-waves and a normal P-R interval.

FIG. 1b.
Warming of the coronary sinus area directly, after opening the right auricle, causes a-v rhythm with simultaneous contractions of auricle and ventricle.

FIG. 1c.
Warming of the coronary sinus area through the coronary sinus vein induces coronary sinus rhythm with gradual increase of the P-R interval and deep negative P-waves.

TABLE I.
P-R Intervals During Sinus Rhythm and During Coronary Sinus Rhythm in 8 Experiments.

Date	P-R during sinus rhythm	P-R during coronary sinus rhythm
3-21-44	.11	.11
4- 4	.08	.08
18	.10	.10-.14
21	.08	.08
28	.08	.08-.10
5-20	.11	.11
2	.08	.08
16	.08	.08

sinus area after opening the auricle always evoked that form of a-v rhythm in which auricle and ventricle contract simultaneously. Since it was possible that in the Langendorff heart local disturbances of circulation prevent normal function of all parts of the a-v node, the experiments were repeated on the dog heart *in situ*.

The heart was exposed after artificial respiration was instituted. Nembutal anesthesia (0.5 cc per kg) was used. The electrocardiogram was registered in lead II. The area around the coronary sinus was warmed by a thermode which was applied through a small opening in the appendix of the right auricle (6 experiments). In order to locate the coronary sinus better, in 17 dogs the vena cava superior and inferior were clamped, the right auricle opened quickly, and the thermode applied to the orifice of the sinus vein especially on its medial aspect. In these experiments only the results obtained within 30 seconds after the clamping of the veins were used in order to eliminate influence due to disturbance of the nutrition of the a-v node. Control experiments showed, that clamping of both venæ cavæ for 50-60 seconds does not influence the length of the P-R interval.

In all experiments thus performed warming the coronary sinus area invariably caused an a-v rhythm in which the auricles and ventricles contracted simultaneously. No inverted P-waves were visible before the QRS-complex.

Different results were obtained however, when the heart was lifted slightly from the pericardial bed and the thermode was pressed on the terminal part of the coronary vein thus warming the area of the coronary sinus from behind. Eight experiments were performed in this way and each time the coronary sinus was repeatedly warmed through the thin wall of the coronary sinus vein or vena cava inferior. Without exception this caused a marked acceleration of the rate and the electrocardiogram showed inverted P-waves at a normal interval before the QRS-complexes.

Fig. 1a was obtained in a typical experiment. A sinus rhythm (rate: 166) exists at the beginning of the tracing. The P-waves are positive and rather high, the P-R interval measures 0.08 second and the QRS-complex shows a very thin, rather short S-wave due to the fact that the apex was slightly lifted from the pericardium. Warming of the coronary sinus through the coronary sinus vein causes an increase of rate up to 230. Deeply inverted P-waves appear and precede the QRS-complex by 0.08 second. The marked, positive Ta-wave moves the ventricular complex slightly above the zero line. The thermode was immediately removed after the cardiac acceleration occurred and the original sinus rhythm is quickly restored.

Fig. 1b shows in the beginning a regular sinus rhythm which was registered after opening the right auricle. Warming of the orifice of the coronary sinus vein induced a short period of tachycardia during which no P-waves were visible because auricle and ventricle contracted simultaneously.

Fig. 1c shows the gradual change from a sinus rhythm to an accelerated coronary sinus rhythm which appeared during warming of the coronary sinus area through the wall of the coronary sinus vein. Due to the tachycardia the P-R interval increases from 0.13 to 0.15 second.

Table 1 shows the P-R intervals during the sinus rhythm and during the coronary sinus rhythm in 8 experiments. In all experiments the P-R distance remained unchanged or became slightly larger during the a-v rhythm. Lengthening appeared at the height of the tachycardia if the thermode was kept in place for a longer time and may be attributed to a fatigue of the conduction to the ventricle.

The experiments prove that stimulus formation in the dog heart, originating in the area around the coronary sinus, is accompanied by inverted P-waves followed by QRS-complexes at a normal interval.

According to Kung[5] the prolongation of the a-v node to the coronary sinus area joins the node on its posterior aspect. It contains many intermuscular ganglion cells. This position of this extension may explain why the warming of area around the mouth of the coronary sinus vein from the endocardial side did not elicit coronary sinus rhythm.

Conclusion. Warming of the area of the coronary sinus in the dog heart ***in situ,*** after opening of the right auricle does not cause coronary sinus rhythm.

This rhythm may be readily elicited if the coronary extension of the a-v node is warmed through the wall of coronary vein.

[5] Kung, *Arch. f. exp. Path. and Pharm.*, 1930, **155**, 295.