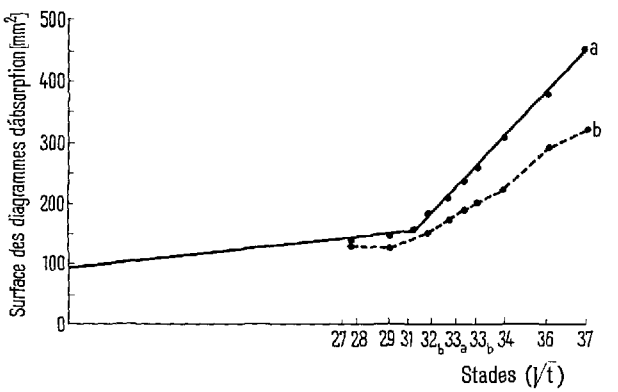
morphologiques commencent à apparaître chez ces derniers. Neuf points de comparaison sont établis depuis le stade 28 (premiers battements cardiaques), jusqu'au stade 37 (percement de la bouche, vitellus résorbé). A chacun des 9 stades examinés, 4 à 6 embryons normaux et un nombre égal d'aneuploïdes sont prélevés individuellement dans des tubes capillaires et soumis à l'extraction suivant la méthode décrite par l'un de nous[1]. Deux extraits d'embryons diploïdes et deux extraits d'embryons aneuploïdes sont soumis parallèlement à l'électrophorèse sur acétate de cellulose (10 V/cm; 1 h de course). Les 4 protéinogrammes résultant d'une même électrophorèse sont ensuite colorés dans un même bain de nigrosine. Grâce à ces précautions, une comparaison qualitative et quantitative est permise entre les spectres électrophorétiques fournis à chaque stade par les embryons normaux et par les aneuploïdes.

Les résultats obtenus ne laissent voir aucune différence significative entre les spectres électrophorétiques donnés par les témoins et par les aneuploïdes. Les bandes constitutives des protéinogrammes embryonnaires apparaissent chez les uns au même moment que chez les autres. L'évolution du spectre électrophorétique se poursuit dans le développement aneuploïde d'une façon tout à fait parallèle à celle qu'a décrite l'un de nous au cours du développement normal[1,2].

Si l'examen qualitatif des protéinogrammes ne révèle aucune différence entre les embryons normaux et les aneuploïdes, par contre l'étude quantitative des mêmes protéinogrammes laisse apparaître une évolution divergente entre les deux types d'embryons. L'examen au photomètre des feuilles d'électrophorèse colorées à la nigrosine permet d'estimer valablement la quantité de protéines extractibles présentes sur celles-ci[2]. Une comparaison photométrique entre les protéinogrammes d'embryons normaux et d'embryons aneuploïdes montre que les seconds fournissent moins de protéines solubles que les premiers. Cette différence est illustrée par la Figure. Les valeurs mesurées pour les embryons diploïdes sont distribuées sur une courbe (a) exprimant l'évolution de la quantité de protéines solubles obtenues par embryon au cours du développement normal. Cette courbe a été établie précédement[1,2]. La courbe (b) est obtenue par référence à la courbe-étalon (a). L'examen de la Figure révèle que les protéines solubles apparaissent plus lentement chez les aneuploïdes que chez les embryons normaux. Un retard significatif s'instaure aux alentours du stade 31, lors de la mise en marche de la circulation sanguine et s'accentue jusqu'au stade 37. Il faut retenir toutefois que la courbe (b) a une simple valeur indicative et n'exprime que l'évolution quantitative globale de la ponte aneuploïde étudiée: celle-ci n'a rien d'une population homogène car chaque embryon aneuploïde est un cas isolé de par sa constitution chromosomique et l'expression du syndrome hyperdiploïde.



Evolution de la quantité de protéines extractibles obtenues par embryon au cours du développement; (a) ponte diploïde; (b) ponte aneuploïde (♂ 3 *n* × ♀ 2 *n*). En abscisse: stades de développement répartis suivant la racine carrée du temps de développement. En ordonnée: mesures de l'intensité de la coloration des protéinogrammes.

En conclusion, les résultats fournis par la méthode électrophorétique indiquent qu'aucune des protéines décelées chez les embryons normaux ne fait défaut chez les germes aneuploïdes. Il se peut toutefois que le déséquilibre chromosomique provoque des troubles de la différenciation protéique, mais qu'ils restent trop faibles pour être décelés par la technique utilisée. Il est donc impossible jusqu'à présent de rattacher le syndrome de l'hyperdiploïdie à une modification qualitative déterminée des structures moléculaires de l'embryon. Mais en tout cas, un effet apparent de l'aneuploïdie est de diminuer la vitesse générale des synthèses protéiques. Ce ralentissement se manifeste à partir du stade 31, moment où la différenciation protéique devient particulièrement rapide chez les embryons normaux[1,2].

Summary. No qualitative differences have been found between the electrophoretic protein patterns observed in normal and in aneuploid embryos (♂ $3n$ × ♀ $2n$). The overall amount of extractable protein increases, however, less rapidly in aneuploid than in normal embryos.

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Effects of Continued Pentaerythritol Tetranitrate Administration on Myocardial Circulation and Metabolism

Therapeutically, pentaerythritol tetranitrate is considered excellent in angina by some clinicians[1,2], while others have found in double blind studies that this compound was not superior to the placebo[3,4]. Opinions as to the efficacy of the agent appear to be related to the method of assessment. It is generally agreed that pentaerythritol tetranitrate relieves angina attacks by preferentially reducing coronary vascular resistance with a resultant increase in the level of coronary blood flow, thus increasing the amount of oxygen available to the ischemic tissue.

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However, only a few reports in the literature have been concerned with acute effects of this agent on myocardial hemodynamics in animals[5–7]; and though RUSSEK[8–10] and WINSOR and HUMPHREYS[11] suggest that pentaerythritol tetranitrate may provide sustained protection against angina attack, there are no data on the effect of continued administration of this compound on myocardial hemodynamics and metabolism, with the exception of the study of JOHNSON et al.[12] in patients with angina. The present report concerns the effects of three weeks of continued administration of pentaerythritol tetranitrate on coronary hemodynamics and myocardial metabolism of the normal anesthetized dog.

Materials and Methods. A series of six experiments were to read performed, one each, on six mongrel dogs ranging in weight from 15.0 to 30.5 kg. Coronary blood flow was determined by the nitrous oxide technique, and other systemic and coronary parameters were determined as previously described[13,14]. Cardiovascular calculations were made after the methods of BING et al.[15]. Statistical analyses were performed using the paired 't' test and the 5% level of significance was accepted.

Following control measurements the animals were given 30 mg of pentaerythritol tetranitrate daily, by gavage, for a period of three weeks. On the 21st day the animals were subjected to the same procedures at which time observations were made before and after the administration of the final dose.

Results. The effects of three weeks of pentaerythritol tetranitrate administration are summarized in the Table. Significant increases were noted in coronary vascular resistance and mechanical efficiency, while reductions were observed in coronary blood flow, cardiac output, left ventricular oxygen consumption and left ventricular work. The coronary fractional flow (coronary blood flow/cardiac output) was decreased 37%. Mean arterial blood pressure remained unchanged. Arterial, pulmonary artery and coronary sinus hematocrits were unaffected during the period of drug administration.

The final dose had a negligible effect on coronary blood flow, cardiac output, coronary vascular resistance, left ventricular oxygen consumption, and left ventricular work when these values were compared to those recorded just prior to its administration. There was, however, a significant increase in respiratory rate from 19 to 42 and in minute volume from 5.37 to 8.39 l/min. The hyperventilation was reflected by a fall in the carbon dioxide tension of arterial, venous and coronary sinus blood which averaged nearly 8 volumes %.

Discussion. Results of the present study suggest that the effect of three weeks of pentaerythritol tetranitrate administration is to increase myocardial efficiency and reduce the cardiac work load, while decreasing coronary blood flow and myocardial oxygen consumption. It would appear that the therapeutic benefit of prophylactic treatment with this compound is due to a sustained reduction in left ventricular work. This conclusion, with respect to

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Alterations in various hemodynamic and cardiovascular parameters as a consequence of the administration of 30 mg of pentaerythritol tetranitrate daily by gavage for a period of three weeks. Experimental values are expressed as mean differences from their respective control values, and were obtained on six dogs before the administration of the final dose

		Control mean	S.E.	Drug mean	S.E.
Coronary blood flow, ml/left vent/min		57.0	10.6	−28.7[a]	6.7
Coronary blood flow, ml/100 g left vent/min		110.2	14.2	−50.3[a]	12.6
Cardiac output, l/min		2.31	0.57	− 0.51	0.23
Oxygen consumption, ml/min		100.1	11.6	−11.3	18.6
Oxygen consumption of left ventricle, ml/min/100 g left vent		13.9	2.00	− 6.47[a]	1.95
Left ventricular work, kg M/min		3.47	0.50	−0.57[a]	0.21
Mean arterial pressure, mm Hg		116	14.5	− 1.4	10.0
Mean pulmonary artery pressure, mm Hg		12.8	3.40	2.28	5.63
Mean coronary sinus pressure, mm Hg		2.70	0.69	− 1.79	1.74
Coronary vascular resistance, units		1.61	0.53	1.07[a]	0.34
Mechanical efficiency, %		32.4	4.8	32.2[a]	10.2
Respiratory rate		18.4	3.4	0.6	10.6
Ventilatory volume, l/min		3.76	1.02	1.71	0.70
Body weight, kg		22.3	–	− 2.3[a]	0.73
Blood oxygen content, vol%	arterial	15.40	1.32	− 0.80	1.16
	coronary sinus	3.75	1.04	0.60	1.00
Blood carbon dioxide content, vol%	arterial	52.12	3.30	− 1.85	2.65
	pulmonary artery	55.16	5.56	− 2.95	2.63
	coronary sinus	60.33	1.76	− 2.56	1.56
Oxygen difference, vol%	arterial-pulmonary artery	4.23	0.33	0.93	0.78
	arterial-coronary sinus	11.66	0.98	− 0.61	1.53

[a] Significant at a level 5% or better.

a lowered work load, is in agreement with those of others based on acute observations in man[16–18].

GORLIN et al.[16,17] reported that nitroglycerin increased coronary blood flow in normal subjects, but not in patients with myocardial insufficiency. These authors proposed that the beneficial effect of this agent in these patients was due to a reduction in cardiac work. In addition ROWE et al.[18] concluded that the primary effect of a longer acting agent, erythrol tetranitrate is to reduce coronary vascular resistance and cardiac work while permitting sufficient coronary flow to sustain the reduced cardiac work load.

However, these results are not in agreement with the findings of others in acute experiments in animals[5,6] in which pentaerythritol tetranitrate produced an increase in coronary blood flow. However, we have reported in a separate communication[7] that in the dog this compound decreased coronary flow, but also decreased cardiac work.

Using a modified radioisotope technique JOHNSON et al.[12] measured myocardial blood flow before and after a single dose of pentaerythritol tetranitrate in 8 angina patients receiving the drug for 2–3 weeks prior to the hemodynamic studies. Myocardial blood flow increased significantly at 2 and 4 h after the last dose when compared to the placebo. The lack of agreement between this and the present study may be related to the animal employed, the administration of anesthesia, the method of evaluating the myocardial circulation, or to the state of the myocardium before drug administration. Nevertheless, the present results point to the difficulty in evaluating agents in experimental animals, by presently useful methods, which are or may be clinically useful in the treatment of myocardial insufficiency.

Zusammenfassung. Die Untersuchungsergebnisse stützen die Vorstellung, dass die gute Wirkung der prophylaktischen Anwendung von Pentaerythritol-tetranitrat bei Patienten mit Coronarinsuffizienz auf Abnahme der Herztätigkeit und Zunahme der Herzmuskelleistung, nicht aber auf eine Zunahme des Coronarkreislaufes zurückzuführen ist.

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Masked Polyphenols in the Cuticle of a Cyst Forming Nematode

The cuticle of the mature female of the potato-root eelworm *Heterodera rostochiensis* Wollenweber is hardened to form a resistant cyst by a tanning process involving a polyphenol oxidase[1]. In histochemical investigation of isolated cuticles, already briefly described[2], the process appears to begin in the outer, fibrous layer, and to proceed inwards to the hyaline, innermost layer ('endocuticle'[3]). Although the tanning agents seem to diffuse inwards, the endocuticle will tan even when isolated. The presence of polyphenols can invariably be demonstrated in the outer region, but it was puzzling that these substances cannot always be detected in the endocuticle; indeed, in 'white cysts' (mature females), it is exceptional for their presence to be demonstrable. MONNÉ[4] has recently shown that

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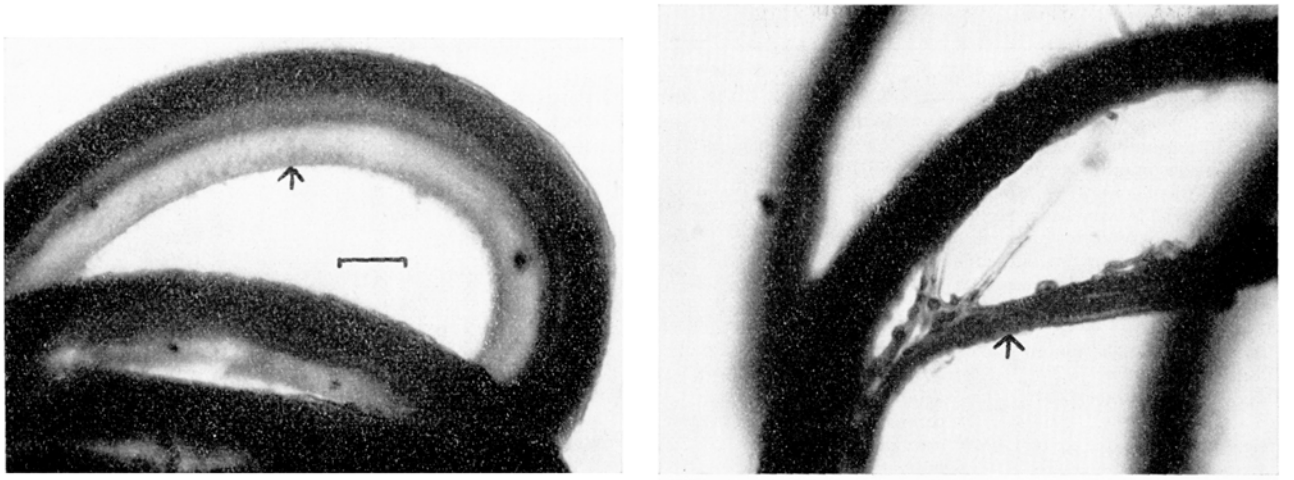

a b

Isolated cuticles held at 60°C for 24 h in water (a), or in methanol-HCl (b); both specimens then treated with ammoniacal silver nitrate for 4 h. → indicates the endocuticle. Scale = 10 μ.