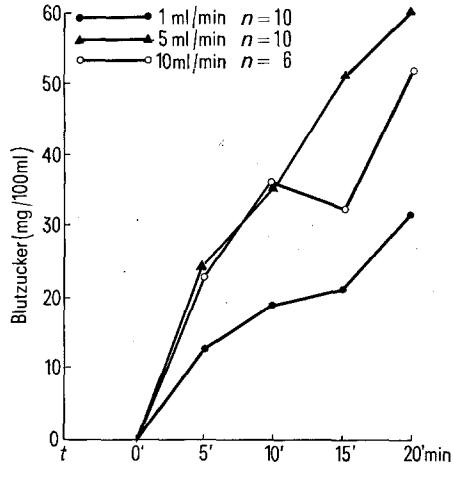
50,3 ± 5,7 mg, das sind 5,3% (Tabelle). Das Verhalten des Blutzuckers ist in der Figur graphisch dargestellt.

Diskussion. Bei statistischer Auswertung (*t*-Test) der resorbierten Glucosemengen bei den verschiedenen Geschwindigkeiten findet sich ein hochsignifikanter Unterschied zwischen den drei Werten ($p < 0{,}01$), vergleicht man hingegen die prozentuellen Werte, so ist statistisch keine Differenz zu sichern ($p > 0{,}1$). Wir interpretieren die Ergebnisse dahingehend, dass bei den gewählten Perfusionsgeschwindigkeiten ein limitierender Einfluss der Kontaktzeit auf die Resorption nicht besteht. Selbst bei der hohen Geschwindigkeit von 10 ml/min kommt es nicht zu einem Absinken der Glucoseresorption oder gar zu einem Sistieren, sondern gegenüber der Gruppe mit langsamerer Perfusion zu einem Anstieg. Dieser Anstieg deutet darauf hin, dass der wesentliche Faktor für die Resorption das Glucoseangebot ist, und dass in unserer Versuchsanordnung das Transportmaximum der Darmwand für Glucose nicht überschritten war. Soweit Analogieschlüsse von tierexperimentellen Ergebnissen auf Verhältnisse beim Menschen zulässig sind, so stehen unsere Resultate in Einklang mit denjenigen von HOLDSWORTH et al.[10], SLADEN et al.[11] und MODIGLIANI et al.[12], welche mittels Perfusion am Menschen zeigen konnten, dass die Menge resorbierter Glucose vom Glucoseangebot an den Dünndarm abhängt. Unsere Ergebnisse stellen hiezu eine Ergänzung dar, da wir mit Absicht auch unphysiologisch hohe Perfusionsgeschwindigkeiten gewählt haben. Sie erklären auch gut die Frage, warum es bei sogenannten funktionellen Diarrhoen, welche mit einer Passagebeschleunigung durch Hypermotilität einhergehen, nicht zu Nutritionsstörungen kommt[13]. BAGLIN et al.[14] konnten an einer Patientengruppe mit solchen Diarrhoen keine Verminderung der Glucoseresorption nachweisen.



Mittelwerte des Blutzuckeranstieges während Perfusion eines Dünndarmstückes (jejunum) mit 0,5%iger Glucoselösung in verschiedenen Geschwindigkeiten.

Wenn unsere Versuche zeigen, dass auch sehr hohen Durchflussgeschwindigkeiten und somit einer verkürzten Kontaktzeit im Dünndarm keine die Resorption limitierende Bedeutung zukommt, so mutet dieses Ergebnis zunächst überraschend an. Betrachtet man den Vorgang der intestinalen Resorption jedoch nicht von der Seite des zu resorbierenden Chymus sondern von der Seite der Dünndarmepithelzelle, so erscheint es doch plausibel, dass es für die resorbierende Zelle gleichgültig ist, ob sich zu resorbierende Stoffe in Ruhe oder in Bewegung befinden, da für den Eintritt eines Moleküls in den für die Resorption verantwortlichen chemischen Mechanismus nur Bruchteile von Sekunden erforderlich sind und auch ein rasch vorwärts getriebener Chymus im Vergleich zur Geschwindigkeit chemischer Reaktionen noch immer als ruhend angesehen werden kann. Ein Einfluss der Kontaktzeit wäre nur bei extrem hohen Passagegeschwindigkeiten denkbar, wie sie im Organismus auch unter pathologischen Bedingungen nicht auftreten.

Summary. Loops of rat's small intestine have been perfused with 5% glucose solution at different flow rates. The absorption of glucose has been investigated. The results showed that, with increasing flow rates, absorption rate of glucose is also increased. Therefore contact time seems to be no limiting factor in intestinal absorption.

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Effect of Generation of Mural Platelet Thrombi on Circulating Blood in Rabbit Aorta

Selective removal of vascular endothelium in anaesthetized rabbits or monkeys is followed by adhesion of blood platelets to the subendothelial surface[1,2]. Within 10 min, numerous platelets accumulate on adhering platelets to form mural platelet thrombi (Figure 1). After 1 h or so, the thrombi have disappeared again[3], thus indicating that thrombi are carried away as white bodies by the blood stream. A similar dynamic process has been directly observed with the light microscope in traumatized vessels of the mesentery[4], the cerebral cortex[5] and the rabbit ear chamber[6].

The present study was undertaken to investigate the effect of mural platelet thrombus formation and disappearance on different parameters of the circulating blood such as platelet count, platelet volume, release of platelet factor 3-like activity, hematocrit and hemoglobin. Blood was collected before and after passage of the thrombogenic subendothelial surface.

Materials and methods. Seven rabbits (weisser Kunath) of either sex weighing 3.0–4.5 kg were pretreated with 10 mg i.p. diazepam and anaesthetized with 30 mg/kg

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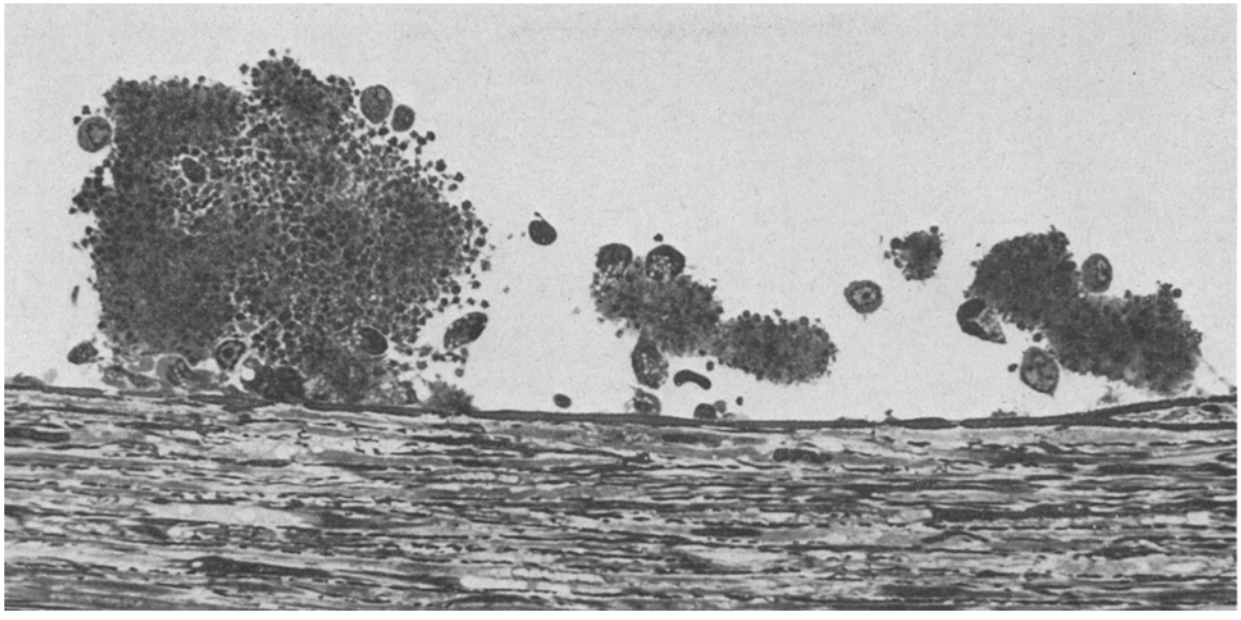

Fig. 1. Micrograph of a 0.8 μm thick epon section of rabbit aorta which had been denuded of endothelium 10 min prior to perfusion with fixative. A large and two small platelet thrombi adhere to the internal elastic lamina. ×800.

pentobarbital. A carotid artery and the left femoral artery were cannulated with silastic® tubing[7]. Blood was allowed to flow from these cannulas as a jet and was collected at intervals as follows. The first 1–2 ml were discarded into a graduated tube (to have an estimate of total blood loss), the following $^1/_2$–1 ml were collected into a small plastic dish for platelet counts; an additional collection was made into Na-citrate (1% final concentration) approximately 10 min before and 10 min after removal of the endothelium for the other determinations. Platelet count and platelet volume distribution were measured with a Coulter Counter Model B as previously described[8], platelet factor 3-like activity according to the method of MacKenzie et al.[9].

The endothelium of an iliac artery, the abdominal and the thoracic aorta were removed by means of a balloon catheter[1,10]. In control experiments the balloon catheter was introduced into one femoral artery but not moved up into the aorta (sham operation). Up to 30 min before, and up to 1 h after denudation of endothelium or sham

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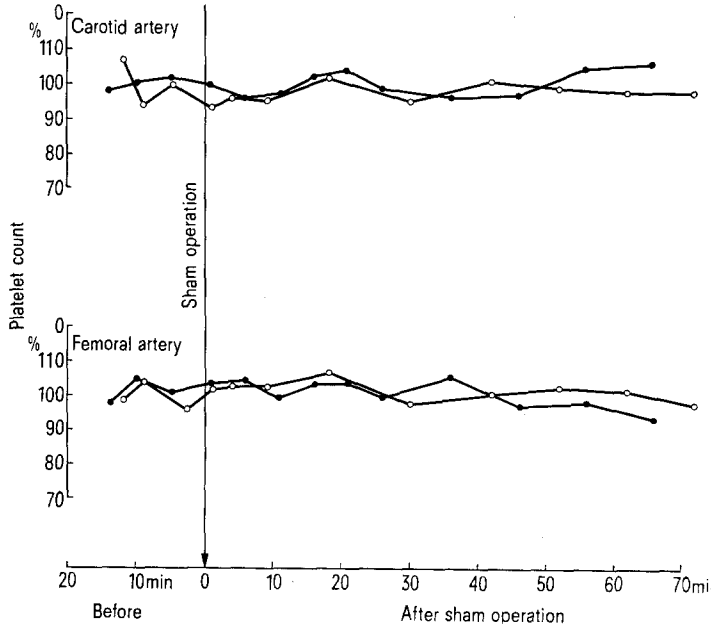

Fig. 2. Platelet counts before and after sham operation in 2 control rabbits. Individual counts are expressed in percent of the average count before sham operation.

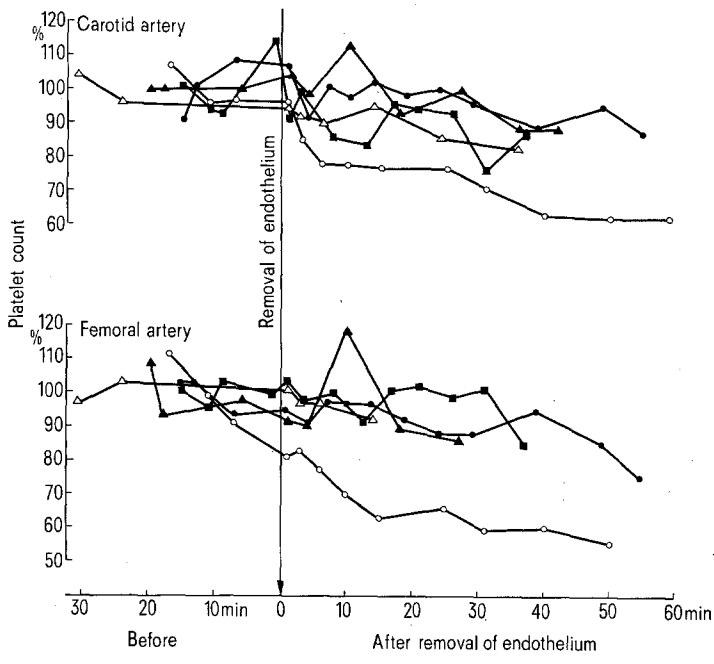

Fig. 3. Platelet counts before and after selective removal of endothelium of rabbit aorta. Platelets were counted in blood collected from the carotid and the femoral artery, i.e. before and after passage of the thrombogenic subendothelial surface. Individual counts of 5 rabbits are expressed as indicated in Figure 2.

operation in the controls, blood was collected at intervals from both silastic cannulas. Blood loss of an animal during the experiment amounted to up to 40 ml. At the end of an experiment the rabbits were sacrificed by injection of an overdose of pentobarbital. Both iliac arteries, a segment of abdominal aorta and a segment of thoracic aorta were dissected, fixed in 4% formalin and processed for histology.

Results. In control experiments the platelet counts remained virtually unchanged (Figure 2) despite the considerable blood loss with a corresponding decrease of hemoglobin and hematocrit of 14–21%. Platelet volume distribution and platelet factor 3-like activity were similar before and after sham operation.

The balloon catheter lesion resulted in virtually complete denudation of endothelium of iliac artery and abdominal aorta in all 5 rabbits of this study, as revealed by light microscopy of histological sections. Denudation of endothelium of the thoracic aorta was partial. In 4 out of 5 rabbits no dramatic or consistent platelet consumption was measurable in the blood which passed over the thrombogenic lesion (femoral artery), neither in absolute terms nor as compared to blood before it passed over the lesion (carotid artery) (Figure 3). However, the platelet count appeared more variable than in controls. In 1 animal the platelet count declined in blood from both carotid and femoral artery. In this and the other animals, no change in platelet volume distribution and platelet factor 3-like activity in the platelet-poor plasma was measured. Hemoglobin and hematocrit decreased by 12–22%.

Discussion. These findings establish that in large arteries acute formation of mural platelet thrombi, which is followed by embolization of white bodies, does not cause measurable alteration of platelet count, platelet volume or release of platelet factor 3-like activity. At least two considerations may help to explain this primarily unexpected finding, namely: a) Platelets consumed or lost by bleeding may rapidly be replaced by new platelets or by platelets from a storage site. The constant level of platelet counts in control animals (Figure 2), despite considerable hemodilution, supports this view. b) The estimated number of platelets involved at the thrombogenic surface is small in comparison with those present in the blood which circulates through the rabbit aorta in a given period of time. This second point deserves more detailed discussion.

The thrombogenic surface of rabbit aorta amounted to approximately 25 cm^2 assuming 4 mm average inner diameter and 20 cm length of denuded aorta. Previous investigations have shown that the subendothelial surface is covered with a platelet carpet which on the average consists of 5 platelet layers after 10 min. In addition mural platelet thrombi which may on the average protrude 25 μm into the vessel lumen, form at 20% of the surface[3]. Assuming furthermore that a platelet covers a surface of 5 μm^2 and is 1 μm thick, the total number of platelets adhering to the vessel wall within 10 min amounts to 4.5×10^9 platelets. In anaesthetized rabbits the platelet concentration approximates 4.5×10^8 platelets/ml blood, and the average blood flow velocity amounts to 50 ml/min[3]. Thus the lowering of platelet concentration caused by the thrombogenic surface is around 2%. This figure lies within the possible error of the counting procedure. On the other hand, the method used to assess platelet factor 3-like activity is very sensitive[8]. Had all platelets adhering to the denuded vessel wall released a major part of their platelet factor 3-like activity, this should have been detected in the platelet-poor plasma. The fact that no measurable amounts of platelet factor 3-like activity were present indicates that most of the platelet factor 3-like activity present was not released from the granules and membrane storage sites of the adhering platelets.

Our data indicate that acute consumption of blood platelets caused by a vascular lesion of limited size usually does not reflect in measurable parameters of the circulating blood, even if measured immediately after passage of a thrombogenic surface. On the other hand, it has been well established that humoral agents which either directly produce intravascular aggregation, such as free fatty acids[11] and adenosine diphosphate[12], or which may

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cause a generalized vascular lesion followed by platelet adhesion and aggregation, such as endotoxin[13], produce dramatic platelet consumption, i.e. severe thrombocytopenia.

Zusammenfassung. Die Innenseite von Kaninchenaorten wurde durch selektive Endothelentfernung in vivo in eine thrombogene Oberfläche verwandelt. Trotz Akkumulation von mehr als 10^9 Plättchen in 10 min an subendothelialen Strukturen konnte keine Veränderung der Zahl, Volumenverteilung oder Faktor-3-Freisetzung von Plättchen im Blut vor und nach Passage dieser Oberfläche gemessen werden.

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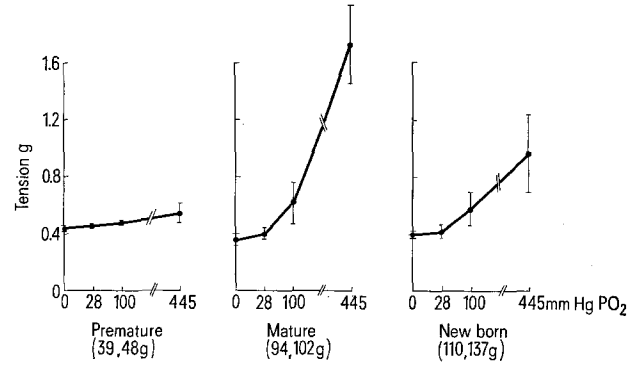
Development of the Q_2 Induced Contractions in the Ductus Arteriosus of the Guinea-Pig

The ductus arteriosus of several animals and man contracts when the PO_2 of the supporting medium is increased. This response constitutes a possibly essential step in the physiological ductal closure after birth and initiation of breathing[1]. The extent of the contraction[2] and the sensitivity to the increase in the O_2 concentration[3] vary among species. Even within the same species, variability in the response to O_2 has been reported[3]. We have attempted to analyze this problem of differences in responsiveness by studying the fetal age dependence of the reactivity to O_2 and norepinephrine (NE) in isolated ductal rings of the guinea-pig.

The vascular segments were isolated from newborn animals and fetuses of different gestational age. The latter was estimated from the body weight, the degree of hair growth and the somatic response to sensory stimulation, e.g. pinching. The mothers were lightly anesthetized with pentobarbital sodium, supplemented by infiltration of lidocaine into the abdominal wall, and the fetuses were delivered by cesarean operation. The fetus or newborn animal was rapidly decapitated; the chest opened; the heart, lungs, and great vessels removed en masse; and the ductus quickly dissected. A ductal ring, approximately 2 mm long, was excised and mounted between two fine wires, to record isometric tension changes (Statham UC2 load cell transducer and Grass Model 5 polygraph) while superfused with Krebs-bicarbonate solution maintained at 37 °C in an organ bath[4,5]. The resting tension was adjusted to 400 mg by varying the distance between the supporting wires with a micrometer. This level was below the in situ wall tension (300 mg/mm or 600 mg for a 2 mm segment) calculated using a simplified Laplace relationship. Changes in tension were evoked by increasing stepwise the PO_2 in the perfusing medium from 0 to 28 (the usual fetal level) to 100 and finally to 445 mm Hg, and also by adding NE (10^{-10} g/ml) to the superfusate.

The graded responses to changes in O_2 increased with the gestational age (Figure) from a very small tension development in the immature fetus to a marked contrac-



Progressive contractile response to increasing O_2 concentration (mean ± S.E.) in the ductus arteriosus of the guinea-pig. Repeated tests (3) were performed in 2 ductal segments from animals at different stages of development. Numbers in parentheses indicate the weight of the fetuses (premature or mature) and the newborn animals. Resting tension, at 0 mm Hg PO_2, was set in all cases at 0.4 g.

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Ductal contraction to NE as a function of PO_2 and maturation

Developmental stage	Premature			Mature			Newborn		
PO_2 (mm Hg)	28	100	Δ	28	100	Δ	28	100	Δ
Change in tension (mg)	45	60	15	75	210	135	60	130	70
to norepinephrine (10^{-10} g/ml)	55	120	65	105	220	115	75	140	65

Change in tension of 6 ductal rings in response to NE. Resting tension in all cases was set at 400 mg. Each ring was tested at low (28 mm Hg and high (100 mm Hg) PO_2. Δ = difference between responses at the two PO_2 levels.