creased growth stimulation.

Summary. Primary hepatic carcinoma, without accompanying cirrhosis or fibrosis of the liver, was induced in rats with diethylnitrosamine. Hyperplastic nodules and nodular cytoplasmic alterations were found in the same livers. Autoradiographs after administration of tritiated thymidine showed no increase in DNA synthesis in morphologically normal areas or in foci of cytoplasmic alterations, but a striking increase in both hyperplastic nodules and carcinoma. It is concluded that primary hepatic carcinoma in the non-cirrhotic liver may arise through stages of increased nodular regeneration.

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Coating of Vascular Surfaces and Cells. A New Concept in Prevention of Intravascular Thrombosis.* (28920)

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Thromboses, arterial and venous, are major clinical problems still inadequately resolved by modern methods of treatment. Among potential anti-hemostatics, macromolecular plasma volume expanders have been known to interfere with clotting(1-4) since 1918, although by mechanisms that are still obscure(5-8). Recently dextran, the most widely used, has been shown to have an antithrombic effect *in vivo*(9,10,11), and *in vitro* it adheres to red blood cells and platelets (14). Infused dextran changes the thrombelastogram as if a defect in platelet function existed, although platelet concentration is not significantly diminished(12,13).

In the dog subjected to standardized arterial trauma by intimectomy of small (femoral) arteries 2.0-3.0 mm I.D., infusion of commercially supplied 6% dextran-saline in amounts equivalent to 10 mg dextran per kg body weight has prevented clotting at the sites of arterial injury(9-11). The anti-hemostatic effect is attributable in part to changes in circulating coagulation mechanisms. It may depend also on changes in luminal vascular surface, particularly at sites of damage. The present data show that C-14 labelled dextran adheres *in vivo* to circulating cells. It also adheres to luminal surfaces of arterial walls especially preferentially at sites of injury.

Procedure. C-14 labelled dextran (characterized in Table I) was used as was commercial dextran in previous experiments(9,11). Dogs were exsanguinated into ACD-solution 30-60 minutes after infusion and, in Experiments B and C, infusions were given just before release of clamps occluding sites of femoral arterial intimectomy.

TABLE I. Radioactive Dextran—Specifications.

Concentration B 512 in saline	6.06 g/100 ml
Molecular wt (light scattering)	82,600 avg
Intrinsic viscosity 25°C	.20
Specific activity (combustion carbon)	6.36 μC/g
Molecules of dextran/disintegration/min	10^{12}
Tagged molecules	1 out of 260
Size—Approx. radial diam.	90 angstroms
" axial "	3,700 "
Counting efficiency	20.1%
Dose injected	1% body wt

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Blood cell suspensions from blood centrifugates and sections of vessels were washed 6 times in commercial dextran-saline. The last wash was free of significant radioactivity. Plasma, washed cells, and blood vessels were digested in strong alkali (KOH in Experiments A and B, LiOH in Experiment C) from which dextran was precipitated and washed with alcohol. The precipitates were plated, dried and counted. Arterial segments were frozen, sectioned parallel to intimal surfaces and then floated from water on to planchets, dried and photographed for planimetric estimation of surface area. Counting efficiency of the gasflow, windowless, proportional counter system used was found to be 20.1% in terms of the dextran-preparation's known radioactivity.

Results. Cell suspensions prepared under similar conditions yielded nearly equal contents of adherent C-14 dextran in 2 experiments. Dextran C-14 also adhered to vessel walls (Table III). Estimates in the latter are quantitatively of like order and differences are presumed to reflect inequalities in sections.

Normal vessel surfaces as compared with symmetrical contralateral segments of like size (Exp. B) and weight (Exp. C) that had been intimectomized, showed greater concentrations of radioactivity at injured than at uninjured sites (Table III).

TABLE II. Radioactivity in or on Formed Elements.

		cpm*
Blood vessel, normal	A	9 ± 1.7
	B	14.5 ± .2
	C	41.0 ± 1.0
1 ml packed washed cells	B	51.2
	C	50.0 ± .2

* Counts per min.

TABLE III. Radioactive Dextran on Normal and Intimectomized Blood Vessels.

	Normal B.V.	Intimectomized B.V.
Exp B	14.5 ± .2 cpm Approx 1 cm²	30.3 ± .2 cpm Approx 1 cm²
Exp C	41 ± 1.0 cpm Weight 49 mg	53.4 ± 1.0 cpm Weight 50 mg

TABLE IV. Radioactivity on Blood Vessel Surface.

	Intima section	Muscular section
Surface area	.098 cm²	.512 cm²
cpm	.35 ± .9	0 ± .09
1 square cm	36 cpm	0 cpm

Distribution of the C-14 dextran was examined in sections of intact aorta (Fig. 1), sectioned before counting into intimal and muscular layers. Activity was found only in the intimal layer (Table IV).

Physical characteristics of dextran molecules (Fig. 2) enabled calculation from these last estimates of the manner of its surface deposition. Concentrations found in aortic intima corresponded to 1.8×10^{14} molecules per sq cm. This is more than would have been found were molecules deposited parallel to luminal surface (estimate $= 3 \times 10^{11}$) but nearly equal to the estimate from radial arrangement with long axes of molecules at

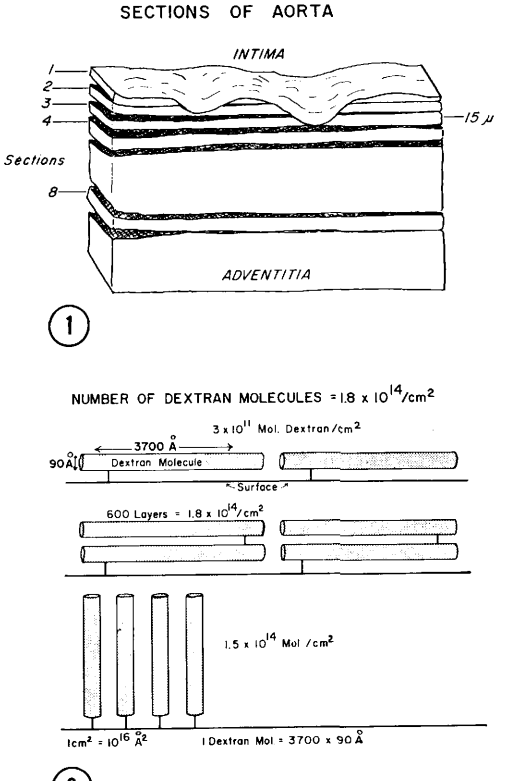

FIG. 1 and 2

right angles to the surface (1.5×10^{14}) assuming saturation of surfaces in both instances.

Comment. Since radioactivity in cell and blood vessel digests was confined to the dextran fraction, it can be assumed that the label was not exchanged. Hence, the experiments show that dextran adheres to circulating blood cells *in vivo* and also on luminal arterial surfaces: in the latter it concentrates at sites of injury (intimectomy) possibly because injury increases surface area. The mechanism by which dextran impairs clotting may therefore be 2-fold, involving changes in properties both of circulating formed elements, such as platelets, and of luminal aspects of vessel walls.

The molecular arrangement which dextran seems to assume on the luminal surface of a vessel is consistent with physical (hydrogen) rather than with chemical bonding. The radial molecular arrangement might direct the terminal-free aldehyde groups of dextran towards the lumen, bending the molecule to the surface. This molecular coating may sterically prevent the achievement of the critical concentration of reactants necessary for clotting or may insulate or counter transmural positive thrombogenic potentials(16) which initiate clotting.

Summary. Infused C-14 dextran adheres *in vivo* to circulating blood cells and also to intimal surfaces of arteries, and in the latter to a greater extent at sites of recent injury. Coating of circulating cells, as well as the intima by dextran molecules (apparently radially arranged on blood vessel surfaces) may participate in the antihemostatic effects of dextran, especially at sites of high concentration consequent on vascular damage.

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Effect of Hypertonic Sodium Nitrate Solutions on Blood Pressure of Rats.* (28921)

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It is well known that excessive ingestion of sodium chloride is accompanied by elevation of blood pressure of both rats and man (1-4). It makes little difference whether sodium chloride is ingested by way of food or drinking water or whether adrenal glands are

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