optically equilibrated D-glucose and 5% β-D-glucose (fig. 1). No statistically significant differences between the spontaneous levels of discharge 0, 1 and 2 min before injection were observed in the α-D-glucose, equilibrated D-glucose, β-D-glucose and saline groups (fig. 2). In the saline group, the level of discharge did not change after the injections. In the α-D-glucose and equilibrated D-glucose groups, the levels of discharge 1 min after the injections decreased significantly ($p < 0.05$) to the levels before injection. The injection of β-D-glucose caused a further decrease in the discharge level; the levels of discharge were suppressed significantly 1 and 2 min ($p < 0.001$ and $p < 0.01$) after administration of the glucose and the decreases were significantly greater ($p < 0.05$–0.01) than those in the α-D-glucose and equilibrated D-glucose groups (fig. 2).

Afferent hepatic vagus discharge in the rat has been shown to decrease transiently after D-glucose injection into the portal vein (figs. 1 and 2). This gives support to the result of Niijima[2]. Regarding the physiological function of D-glucose anomers; several studies have disclosed that β-D-glucose is more rapidly taken up and metabolized by various cells and tissues than α-D-glucose[7–9]. Anatomically, hepatic afferent sensory nerve fibers have been identified as free nerve endings[10]. Since β-D-glucose was most potent in reducing the nerve discharge (fig. 2), the action of D-glucose on the hepatic nerve terminals seems to be predominantly due to an action of D-glucose on the intracellular glucose metabolism. These observations suggest that activation of hepatic glucosensitive mechanisms is dependent on the anomeric stereospecificity of D-glucose in the blood.

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The role of volume expansion, of prostaglandins and catecholamines in the development of acute renal failure

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Summary. A single injection either of isotonic or hypertonic saline solutions protected rats against acute renal failure (ARF) induced with glycerol. This protection was accompanied by increased urinary prostaglandin E (PGE) concentration. On the contrary, a single s.c. injection either of hypotonic saline or isotonic glucose solution, which did not increase urinary PGE concentration, or depletion of the endogenous catecholamines, using reserpine, did not protect the animals against acute renal failure.

In previous studies it has been observed that infusion of PGE_1 and PGE_2 partially protected the rats against ARF induced with glycerol[2,3]. On the other hand Wilson et al.[4] found out that volume expansion protected the rats against ARF. Since it had been observed that 1. volume expansion either of the intravascular or the extracellular space stimulated renal prostaglandin (PG) synthesis in rats[5,6] and dogs[7] 2. the increased release of PGs following volume expansion diminished in binephrectomized rats 3. the concentration of PGs in rat, rabbit an dog kidney (rather the capacity of renal tissue to synthetize PGs) is high[8–10], it has been suggested that 1. the kidney is the major source of PG synthesis and 2. renal PGs must play important rôle in the development of ARF. These suggestions have been strengthened by the observation that a PG synthesis inhibitor (indomethacin) enhanced ARF in rabbits[11] and prevented the protective effect of saline against ARF in rats[12] and moreover the addition of PGE_2 to a saline infusion restored its protective effect[12].

In these studies we investigated 1. whether the protective effect of saline against ARF is accompanied with an increased urinary PGE concentration, 2. whether the injection of isotonic glucose solution (which decreases PG synthesis)[13] protects the animals against ARF, and 3. whether the depletion of catecholamines, using reserpine, protects the animals against ARF. Our results are suggestive of a) an involvement of renal prostaglandins in the protection afforded by saline, b) an insignificant role of catecholamines in the development of this model of ARF.

Material and methods. Male Wistar rats 200–250 g (mean 221 ± 3 g) were used in this study. The animals were randomly allocated to 8 groups, each one consisting of 10 animals. ARF was induced by single s.c. injection in the anterior abdominal wall of 10 ml kg^{-1} of 50% (v/v) glycerol solution. The animals were subsequently deprived of food and water throughout the investigation. 24 h collections of urine were made, using metabolic cases.

Group 1 (G 50%): The rats were injected only with glycerol (50% 10 ml kg^{-1}). Group 2 (GG): The animals were injected with glycerol and isotonic glucose solution (75 ml kg^{-1}). Group 3 (GS 4.5 g l^{-1}): The animals were injected with glycerol and hypotonic saline (4.5 g l^{-1}, 75 ml kg^{-1}). Group 4 (GS 9 g l^{-1}): The animals were injected with glycerol and isotonic saline solution (9 g l^{-1}, 75 ml kg^{-1}). Group 5 (GS 18 g l^{-1}): The animals were injected with glycerol and hypertonic saline solution (18 g l^{-1}, 75 ml kg^{-1}). Group 6 (GS 150 g l^{-1}): The animals were injected with glycerol and hypertonic saline solution (150 g l^{-1}, 5 ml kg^{-1}). Group 7 (GR): The animals were pretreated with reserpine 4 days before they had been injected with glycerol in order to deplete catecholamines (2×0.5 mg kg^{-1} day^{-1} for 4 days). Group 8 (GRG): The animals were treated as those of the 7th group and injected with isotonic glucose solution (75 ml kg^{-1}) before they were injected with glycerol.

All solutions were given by single s.c. injection. 24 h after glycerol injection the animals were anesthetized with ethylbutylbarbiturate (mebubarbital ABBOTT, 30 mg kg^{-1}) i.p. The animals were also given heparin (600 units kg^{-1} in 1-3 ml of saline per kg). The right carotid artery was catheterized and blood was collected in a plastic tube for estimation of endogenous true creatinine.

The following parameters were measured. 1. Urinary and plasma creatinine concentration, by a method described in detail elsewhere[14], using Fuller's earth for non-chromogen creatinine estimation. 2. Urinary and plasma uric acid, by the method of Sobrinho and Moes[15]. 3. Urinary PGE concentration was measured by a radioimmunoassay (RIA) method (Clinical Assay Kits, Cambridge, Massachusetts). The procedure used for extraction and quantitative RIA estimation is described in detail elsewhere[16].

Results. The results are summarized in the table. The single s.c. injection of isotonic glucose solution (group 2) and of hypotonic saline (group 3) in the rats did not prevent the development of ARF. Thus plasma creatinine (Pcr) concentration, clearances of creatinine (Ccr) and uric acid (Cua), urine volume (UV) and urinary PGE concentration (which reflects the renal PG synthesis)[17] did not differ significantly compared to the values obtained in the 1st group injected only with glycerol (table).

On the contrary, the single s.c. injection either of isotonic (group 4) or hypertonic saline solutions (group 5 and 6) in the rats protected the animals against ARF. Thus Pcr concentration was significantly lower and Ccr, Cua, UV and urinary PGE concentration were significantly higher when the values obtained were compared to those of the 1st group injected only with glycerol. Finally, depletion of the endogeneous catecholamines, using reserpine, did not protect the animals against ARF whether injected or not with isotonic glucose solution; group 8 and 7 respectively.

Discussion. Glycerol injected s.c. or i.m. decreases renal plasma flow (RPF) and glomerular filtration rate (GFR) and causes haemoglobinuria, oliguria and severe azotemia in rats. Volume expansion was found to prevent oliguria and greatly to decrease the death rate of glycerol injected rats[4]. In our experiments we observed that volume expansion protected the animals against ARF and that the protection was accompanied by increased urinary PGE concentration. On the other hand, isotonic glucose solution and hypotonic saline did not protect the animals against ARF and did not increase urinary PGE concentration (table). It is suggested that volume expansion, by increasing PGE and by decreasing renin-angiotensin II play an important role in the protection of the animals against ARF, induced with glycerol, because of the following findings; 1. PGE and PGI_2 infusion increased renal plasma flow, non cortical plasma flow (NCPF) urine volume (UV) and sodium excretion rate in animals and in human beings[18-22], and protected the rats against ARF[2,3,12]; 2. PGs are formed in both renal medulla and cortex[8-10,23]; 3. intravascular and extracellular space expansion increased RPF, NCPF, UV, and urinary and plasma PGs[5-7,24,25] and diminished renin release[26,27]; 4. the increased release of PGs following volume expansion diminished in binephrectomized animals[5,6], and 5. isotonic and hypertonic saline solutions increased renal microcirculation by increasing the circulating blood volume.

The increase of urinary PGE concentration following volume expansion could be the result of an increase of renal PG biosynthesis and/or of an increase of the circulating blood volume and mainly of RPF and NCPF. In any case, the increase of the circulating PGE further improved renal microcirculation by dilating the afferent arteriole.

The role of catecholamines in the development of this model of ARF seems to be unimportant. Thus the animals of the groups 7 and 8 which were pretreated with reserpine (depletion of the endogenous catecholamines) were not protected against ARF. These findings are in accordance with those of Eliahou, Brodman and Friedman[29] who have found out that ARF could be induced in denervated transplanted kidney and was not prevented or reversed by adrenergic blockades.

In conclusion, the possible involvement of multiple factors in the depressed renal function of glycerol-induced ARF complicates the investigation of its pathophysiology. However, the present findings could indicate that volume expansion increased the circulating blood volume and the vasodilator PGE, and prevented the increase of renin

Table. The effect of isotonic glucose solution, of hypotonic, isotonic and hypertonic saline solutions and reserpine on plasma creatinine (Pcr) concentration, clearance of creatinine (Ccr), clearance of uric acid (Cua), urine colume (UV) and urinary prostaglandin E (PGE) concentration during acute renal failure (ARF) induced with glycerol in rats

Group	1 G 50% (10 ml kg^{-1})	2 GG (75 ml kg^{-1})	3 GS 4.5 g l^{-1}	4 GS 9 g l^{-1}	5 GS 18 g l^{-1}	6 GS 150 g l^{-1} (5 ml l^{-1})	7 GR	8 GRG (75 ml kg^{-1})
Pcr	23.660	29.340	27.310	10.500	7.500	12.300	22.250	28.800
SEM (mg l^{-1})	3.606	3.540	4.970	1.374	0.445	1.212	3.314	2.462
p		NS	NS	0.01	0.01	0.01	NS	NS
Ccr	0.526	0.327	0.567	2.358	2.048	2.083	0.752	0.330
SEM (ml kg^{-1} min^{-1})	0.192	0.154	0.219	0.390	0.202	0.334	0.190	0.076
p		NS	NS	0.01	0.01	0.01	NS	NS
Cua	0.073	0.090	0.073	0.187	0.271	0.235	0.109	0.126
SEM (ml kg^{-1} min^{-1})	0.027	0.032	0.037	0.036	0.097	0.069	0.028	0.022
p		NS	NS	0.025	0.05	0.05	NS	NS
UV	1.137	1.694	1.577	2.904	3.144	1.804	2.016	2.266
SEM (ml kg^{-1} h^{-1})	0.232	0.760	0.504	0.280	0.265	0.198	0.408	0.415
p		NS	NS	0.01	0.01	0.01	0.05	0.025
PGE	4.563	3.060	3.330	16.830	14.270	14.243	6.633	5.677
SEM (mg kg^{-1} h^{-1})	1.560	1.433	1.900	4.667	4.377	1.190	3.400	1.500
p		NS	NS	0.025	0.05	0.01	NS	NS

G 50%, glycerol 50%, 10 ml kg^{-1}; GG, glycerol + isotonic glucose solution 75 ml kg^{-1}; GS 4.5 g l^{-1}, glycerol + saline 4.5 g l^{-1}, 75 ml kg^{-1}; GS 9 g l^{-1}, glycerol + saline 9 g l^{-1}, 75 ml kg^{-1}; GS 18 g l^{-1}, glycerol + saline 18 g l^{-1}, 75 ml kg^{-1}; GS 150 g l^{-1}, glycerol + saline 150 g l^{-1}, 5 ml kg^{-1}; GR, glycerol + reserpine 2 × 0.5 mg kg^{-1} day^{-1} for 4 days; GRG, glycerol + reserpine 2 × 0.5 mg^{-1} day^{-1} for 4 days + isotonic glucose solution 75 ml kg^{-1}. The values of PGE were corrected with the mean recovery obtained of the added PGE_2 in the urine. All values were compared against those obtained in group 1 injected only with glycerol.

release. These agents prevented a decrease of the RPF and mainly of the GFR and consequently protected the animals against ARF. Nevertheless, further investigation must take place and more parameters must be measured simultaneously, mainly those concerning renal circulation, the blood pressure, the release of the prostaglandin F (PGF_{2a}) (which inhibits renin release[30,31] and facilitates venous circulation[32]) and thromboxane A_2 (TXA_2) (which is a potent vasoconstrictor agent[33]).

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Enhancement of the sensitivity of hamster cheek pouch arterioles to beta-adrenergic stimulus during pregnancy

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Summary. The adrenergic beta stimulant fenoterol induced a dose-dependent vasodilatation of hamster cheek pouch arterioles. The response to fenoterol was significantly larger on day 14 of pregnancy than in metoestrous animals. Since the serum progesterone and 17 beta-oestradiol level were also elevated on day 14, a relationship was suggested between the enhancement of vascular sensitivity and sex-steroid hormone levels.

Sex-steroid treatment is able to modify the sensitivity of arterioles to catecholamines[1-4]. As the blood level of sex-steroids increases during pregnancy a change in the sensitivity of arterioles can be expected to beta-adrenergic stimulus. Thus we have studied a) whether the sensitivity of arterioles to beta-adrenergic stimulus changes during pregnancy, and b) whether the change in sensitivity is connected with the increase in sex-steroid plasma level.

Materials and methods. Golden hamsters weighing 90–140 g were maintained on 13 light and 11 dark photoperiods. The regular 4-day oestrus cycle was determined by a postovulatory vaginal discharge. $^2/_3$ of the animals were put together with fertile males on a proestrus afternoon and the following day the sperm positive females were considered as day-1 pregnant.

Microcirculatory study was performed under pentobarbital (60 mg/kg; May and Baker) anesthesia on day 6 or day 14 of the pregnancy (hamster pregnancy is 16 days); metoestrous animals served as controls. The cheek pouch membrane of animals was fixed on a special table and placed under a Zeiss microscope. In order to prevent the drying out of the membrane a small quantity of physiological saline solution was infused continuously into the cheek pouch by a peristaltic pump. Arterioles ranging in size from 30 to 60 µm were selected for study and a short-circuit television (Siemens) was applied to reach an appropiate magnification (×500–1500). Fenoterol (Partusisten, Boehringer) in doses of 0.25, 0.5 or 1.0 µg was topically applied and 20, 40 and 60 sec after its administration, the changes of the inner diameter of the arterioles was measured using a scale on the screen of the television. Then the membrane was washed out and the next dose was randomly administered 5 min later.

Following the microcirculatory study, blood was taken