preparation used. It should, however, be noticed that Grantham and coworkers use a preparation which seems to have a much lower Na^+ content. New data are awaited to shed light on this problem.

Our results further show that ouabain (10^{-3} M) blocks the swelling limitation process. Maximum swelling achieved in the presence of that compound coincides with that expected, considering a perfect osmometric behavior of the cells (fig. 1). This confirms earlier findings by Paillard et al.[12]. Our data also show that ouabain has no significant effect on the volume readjustment process. The lack of effect of ouabain on volume readjustment has already been reported in a variety of tissues and cell types[4,5,6,8,10]. In these cases however, volume readjustment can be related to a decrease in intracellular content of K^+ and/or amino acids due to an increase in plasma membrane permeability; the fact that ouabain has no effect is therefore not surprising. As far as kidney slices are concerned, our findings indicate that the Na^+ extrusion process concomitant with volume readjustment is not related to the activity of a Na^+/K^+, ouabain sensitive pump. Some other mechanism must therefore take an active part in the process. Further results should solve this problem.

Ouabain blocking of the swelling limitation phase has been considered as evidence that the activity of the ouabain sensitive Na^+/K^+ pump is involved in this process. However, our results show that in hypo-osmotic as well as in isosmotic conditions, ouabain induces a 1:1 exchange of Na^+ for K^+. In both cases, the increase in Na^+ level is indeed compensated by a similar decrease in K^+ and there is thus no net change in the total amount of intracellular osmotic effectors (fig. 3). This can easily account for the fact that ouabain has no effect on the tissue volume in isosmotic conditions. This can also account for the block of the swelling limitation process. Since there is no change in the total amount of osmotic effectors during that phase in the presence of ouabain, the cells behave as ideal osmometers. In this context, the decrease in Na^+ content associated with swelling limitation in the absence of ouabain can be explained simply by considering that 1. swelling limitation involves no change in the stoichiometry of the pump and leak system exchanging Na^+ for K^+ (1:1); 2. the intracellular level of Na^+ is determined by a readjustment of its ratio out/in at control level. In agreement with this is the fact that the ratios Na_o/Na_i remain in the same range in isosmotic conditions and during the swelling limitation phase (1.81 against 1.90 after 30 min of hypo-osmotic shock). It may be worth noticing that Na_o/Na_i ratio is much higher at the end of volume readjustment than in isosmotic conditions or during swelling limitation (3.11 against 1.81 or 1.90). This indicates that different processes are probably at work in the control of the Na^+ level in swelling limitation and in volume readjustment.

Studies on the mechanisms of Na^+ regulation implicated during that last phase are in progress in this laboratory.

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Cardiovascular compensatory and decompensatory responses in rats anesthetized with pentobarbital compared to chloralose-urethane[1]

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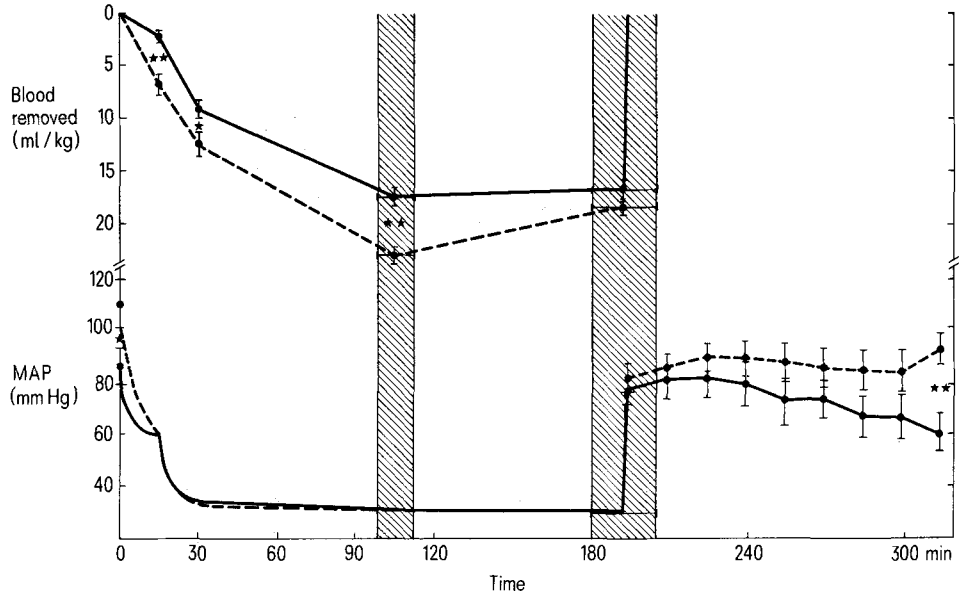
Oral Roberts University, Tulsa (Oklahoma 74171, USA), October 29, 1982

Summary. The data presented in these studies suggests that rats anesthetized with pentobarbital are better able to compensate for acute blood loss, but are less able to sustain the compensatory effort during hemorrhagic hypotension than rats anesthetized with chloralose-urethane. However, following reinfusion of shed blood the pentobarbital rats are better able to maintain their blood pressure.

One of the most important decisions facing biomedical scientists who use animals in their studies is whether or not the animals will require anesthesia; and if they do, which anesthetic or anesthetic regime is best suited for their particular study. In order to make a rational choice, one must be aware of the many side effects that accompany the use of anesthetics. For example, all anesthetics possess a CNS depressant action which places the animals in a state of unconsciousness and presumably renders them insensitive to painful stimuli. However, some anesthetics have been reported to have a greater depressant effect on discrete areas of the CNS than others, thus making them unsuitable for certain types of physiological investigation. For example Ruffy et al.[2] have shown recently that alpha-chloralose is better able to preserve the electrical properties of the heart subjected to reduced flow than secobarbital. In



This graph compares the hemorrhage response of Sprague-Dawley rats anesthetized with pentobarbital (dashed lines) to those anesthetized with chloralose-urethane (solid lines). Each experiment employed 1 rat from each group for a total of 10 pairs. All data is plotted as the mean ± SEM. One star represents a $p < 0.05$, while 2 stars represent a $p < 0.01$. The 1st vertical shaded area at 97–112 min denotes the mean ± SEM for the time to achieve maximal blood loss (i.e. maximal compensatory effort) when MAP is reduced to 30 mm Hg. The 2nd shaded area at 180–205 min indicates the mean ± SEM for 20% uptake in the pentobarbital animals. The chloralose-urethane animals did not progress on to the 20% uptake stage.

an earlier study, Van Citters et al.[3] reported seeing a differential effect on the 2 branches of the autonomic nervous system when the dogs were a) unanesthetized, b) anesthetized with alpha-chloralose, and c) sodium pentobarbital. Their studies indicate that animals anesthetized with sodium pentobarbital had higher heart rates and blood pressures than those anesthetized with alpha-chloralose even though the cardiac work was not different. These authors also report that the animal to animal variability is much reduced with sodium pentobarbital. More recently Zimpfer et al.[4] reported that pentobarbital anesthesia does modify the ability of dogs to compensate for blood loss. Specifically, these authors demonstrated that the sympathoadrenal response, but not the renin-angiotension system, was depressed in pentobarbitalized dogs compared to chronically instrumented unanesthetized controls during acute blood loss. In 1973, Bond et al.[5] published a study which compared the responses of myocardial contractibility, blood pressure, heart rate, respiration rate and total body oxygen comsumption to acute hemorrhage in dogs anesthetized with 3 different regimes. These authors suggest that a combination of droperidol and fentanyl together with a $\frac{1}{3}$ normal dose of sodium pentobarbital produces good surgical anesthesia without the hypertension and tachycardia usually seen with sodium pentobarbital alone. In another study[6], these authors reported that this combination did result in strong alpha-adrenergic blockade, particularly in the skeletal muscle vasculature of dogs.

Therefore, there is still considerable controversy concerning the most appropriate anesthetic for studying the cardiovascular responses to hemorrhagic shock. The following study was designed to compare the total body compensatory and decompensatory cardiovascular responses of the rat to a modified Wiggers' shock protocol using 2 anesthetic regimes (sodium pentobarbital and a combination of alpha-chloralose and urethane).

Methods. All experiments utilized 2 male Sprague-Dawley rats of similar size (approximately 500 g). One of these was anesthetized by administration of 35 mg/kg i.p. sodium pentobarbital, while the others were anesthetized by i.p. injection of a mixture of 80 mg alpha-chloralose and 400 mg urethane per kg. Attempts were made to adjust the level of anesthesia to be equivalent to stage III plane 2[7]. The surgical preparation of each rat included: a) the cannulation of the right femoral vein to permit postsurgical administration of 5 mg/kg heparin sodium; b) the cannulation of the trachea to provide an adequate ventilatory pathway; and c) the cannulation of the right carotid artery of each animal using a PE 50 catheter. These arterial cannulae were connected to T-tubes with one branch leading to a P23Db Statham Pressure Transducer and the other to a 25 ml calibrated buret. The 2 burets (one attached to the carotid arteries of each rat) were connected with tubing in such a way that a well-controlled and equal pressure could be applied to the surface of the fluid in both burets. The experimental protocol consisted of applying a pressure of 60 mm Hg to the fluid surface in both burets. The stopcocks separating the rats arterial pressure and the 60 mm Hg in the burets were then opened allowing the movement of blood from the arterial circulation of the rats into the buret until the rat pressures equalized to 60 mm Hg. After stabilization the buret pressure was lowered to 30 mm Hg where it was held until one of the rats decompensated to the point of requiring 20% reuptake from the buret in order to maintain 30 mm Hg arterial pressure. At this point both animals were simultaneously reinfused by applying pressure to the fluid surface. Both rats were then monitored for an additional 2 h. A total of 10 experiments are reported which had one rat from each group. All data is presented as the mean ± SEM. The level of significance was determined using the paired Student's t-test. Probability values between 0.01 and 0.05 are noted on the figure with 1 star, while values less than 0.01 are noted with 2 stars.

Results. As can be seen in the accompanying figure, the prehemorrhage control mean arterial pressures (MAP) were higher in the sodium pentobarbital group (108 ± 8 mm Hg) than the chloralose-urethane group which

was only 86±7 mm Hg. However, as can be seen in the upper panel, the blood loss necessary to lower the MAPs to 60 and 30 mm Hg were significantly higher in the pentobarbital group (6.8±0.9 ml/kg and 12.6±1.4 ml/kg) than in the chloralose-urethane group (2.3±0.4 ml/kg and 9.2±0.8 ml/kg). In addition, the maximum shed volume during compensation which occurred during shaded area around 105 min was also significantly greater in the pentobarbital group (23.1±0.8 ml/kg) compared to the chloralose-urethane group (17.6±0.8 ml/kg). Also of significance was the fact that in each of the 10 sets of experiments the pentobarbital series decompensated to 20% utpake while the chloralose-urethane rats failed to exhibit this type of cardiovascular decompensation. Upon restoration of normal blood volume, the MAPs of both groups returned toward control; however, after 2 h only the pentobarbital group was able to maintain this pressure.

Conclusions. The fact that the prehemorrhage control MAP was higher in rats anesthetized with pentobarbital than chloralose-urethane suggests that choralose-urethane has less of an effect on blood pressure control than pentobarbital. However, these rats were able to lose significantly more blood at 60 and 30 mm Hg than the chloralose-urethane group suggesting that they are better able to compensate for acute blood loss. This compensatory effort noted in the pentobarbital group progresses into cardiovascular decompensation as seen by the uptake of blood between 105 and 190 min but not in the chloralose-urethane group. The fact that the chloralose-urethane animals were unable to maintain their blood pressure 2 h postreinfusion suggests that these animals were more severely compromised during the hemorrhagic hypotensive phase of the experiment even though they bled less and did not show cardiovascular decompensation, (i.e. take back blood from the buret) during hypovolemic hypotension (180 to 205 min in the fig.).

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Enhancement of human neutrophil oxygen consumption by chemotactic factors[1]

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Summary. Human neutrophils preincubated with chemotactic factors showed enhanced OPZ-induced oxygen consumption. Maximum capacity of neutrophils to consume oxygen was found to be limited for both FMLP-treated cells and control cells. But with lower doses of OPZ, FMLP-treated cells consumed more oxygen than control cells.

Chemotaxis of neutrophils is an important part of the host defense system. Chemotactic factors induce not only chemotaxis but also neutrophil activation, which includes degranulation[2], chemiluminescence[3], superoxide anion production[4] and activation of the hexose monophosphate shunt[5]. Furthermore, preincubation of neutrophils with chemotactic factors enhances the stimulation of superoxide production[6,7], hexose monophosphate shunt activity[8],

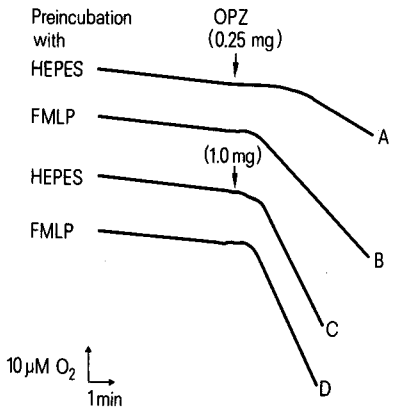

Figure 1. Enhancement of neutrophil oxygen consumption by FMLP preincubation. Tracings illustrate changes of oxygen concentrations in 1.0 ml HEPES-buffer containing 2×10^6 cells at 37 °C. The cell suspension was preincubated for 30 min with either FMLP (10^{-7} M) or HEPES-buffer prior to the addition of OPZ.

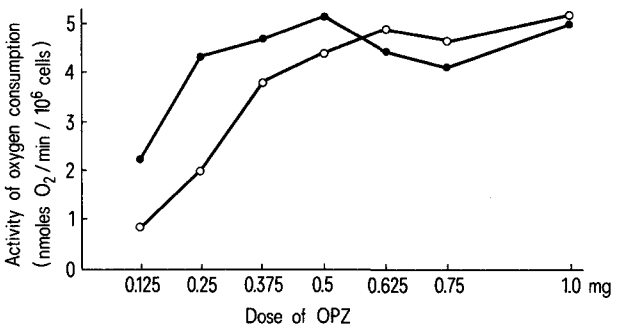

Figure 2. Relationship between the dose of OPZ and oxygen consumption. Neutrophils were preincubated for 30 min at 37 °C with FMLP (—●—) or with HEPES-buffer (—○—). The ordinate indicates activity of oxygen consumption. Representative data are shown from 1 subject.