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Temporal Variations in Testicular Microcirculation

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ABSTRACT: Temporal variations in microcirculatory blood flow in the testis and blood pressure were examined in intact, pentobarbital-anesthetized rats with a two-channel laser Doppler flowmeter. The laser Doppler probes that measure local blood flow in a tissue volume of about 2 mm³ were placed either over the mid portion of the left and right testes or on the right testes 1 cm apart. Testicular microcirculation was characterized by a prominent vasomotion with a frequency of 5.3 ± 1.4 cycles per minute and with an amplitude of 73 ± 32% (mean ± SD) of the mean. In addition to this large and rapid variation in local blood flow, there were also major variations from minute to minute in the average blood flow, vasomotion frequency, and vasomotion amplitude at 40 and 53 minutes. Such variations in local blood flow, vasomotion frequency, and vasomotion amplitude were correlated with each other at two different sites on the same testis (r_s = 0.39, r_s = 0.82, r_s = 0.64, respectively, $P < 0.001$), and they were all correlated with systemic blood pressure (r_s = 0.41, r_s = 0.61, r_s = 0.32, respectively, $P < 0.001$). Minute-to-minute variations in local blood flow, vasomotion frequency, and vasomotion amplitude were also correlated between the right and left testes (r_s = 0.58, r_s = 0.75, r_s = 0.57, respectively, $P < 0.001$). There are substantial temporal variations in testicular microcirculation. These variations are to some extent related to temporal changes in systemic blood pressure, but changes in the ultralocal environment are probably more important. The functional significance of, and the factors responsible for, local variations in testicular microcirculation remain to be elucidated.

Key words: Vasomotion, testis, blood pressure, rats.
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Several physiological processes in the testis, such as testosterone secretion, spermatogenesis (seasonal variations), and contractions of the seminiferous tubules and the testicular capsule show temporal variations with different frequencies. The question of whether local testicular blood flow is constant during normal physiological conditions or whether it also shows temporal variations, variations possibly related to changing local metabolic demands, has not been studied in detail.

Basal testicular blood flow, vasomotion (rhythmic variations in microvascular flow), and vascular permeability are maintained by luteinizing hormone (LH) and testosterone (Bergh and Damber, 1993). Low doses of exogenous LH or endogenous LH pulses do not, however, appear to have acute effects on testicular blood flow (Bergh and Damber, 1993; Setchell et al, 1994), suggesting that physiological temporal variations in Leydig cell function do not induce temporal variations in testicular blood flow. On the other hand, other lines of evidence suggest that testicular blood flow is not constant and that variations in local flow could be related to temporal changes in local demands. These lines of evidence follow. 1) Several rapidly acting (maximal effects within minutes after administration) vasodilators (e.g., ANP, CNP, VIP, PACAP, and CGRP) and vasoconstrictors (e.g., AVP, 5-HT, and ET-1) are secreted locally in the testis. Some of these factors are secreted by Leydig cells, others by mast cells, nerves, or cells in the seminiferous tubules (for review, see Bergh and Damber, 1993; Collin, 1996). 2) The testicular microcirculation is characterized by regular variations in local blood flow of high amplitude (so-called vasomotion; Bergh and Damber, 1993).

Vasomotion, which is induced by regular myogenic activity in arterioles, has been observed in several tissues (Funk and Intaglietta, 1983; Intaglietta, 1988) but apparently nowhere with such a large amplitude as in the testis (Collin, 1996). Vasomotion frequency and amplitude in other organs are influenced by highly local hormonal and neuronal mechanisms but also by systemic factors such as blood pressure (Bouskela and Grampp, 1992; Morita-Tsuzuki et al, 1992; Griffith, 1994; Achakri et al, 1995).

The physiological importance of vasomotion is not known in detail, but it probably influences transvascular fluid exchange and vascular resistance, and it may facilitate tissue oxygenation (Funk and Intaglietta, 1983). In the testis, vasomotion could be of particular importance for the resorption of plasma at the venous side of the microvessels (Bergh and Damber, 1993). The regulation of testicular vasomotion is largely unknown, but vasomotion frequency and amplitude are influenced by changes in testosterone, 5-HT, ET-1, and other locally produced substances (Bergh and Damber, 1993; Collin, 1996).

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Temporal variations in testicular blood flow could also be related to changes in systemic blood pressure or other systemic factors. Average total testicular blood flow is correlated to systemic blood pressure in anesthetized rats (r = 0.64, Free, 1977; Damber, 1978). In contrast, Davis (1990, 1992) observed signs of autoregulation in the isolated testicular rat artery. The question of to what extent testicular blood flow is related to blood pressure is therefore unresolved.

The aim of this study was to examine whether there are temporal variations in local blood flow, vasomotion frequency, and vasomotion amplitude in the rat testis and to explore to what extent such variations are due to systemic and local control mechanisms.

Materials and Methods

Animals, Treatment, and Anesthesia

Adult male Sprague-Dawley rats weighing 350–400 g were purchased from ALAB Laboratorietjänst AB, Stockholm, Sweden. The animals were kept in a local animal house with free access to standard pelleted food and water. Anesthesia was induced by intraperitoneal injection of pentobarbital (Mebumal; ACO, Solna, Sweden, 40–50 mg/kg body weight).

Experimental Procedure

The animals were placed on a heated pad (32°C). The testes were exposed by scrotal incisions and were immobilized by placing them in small bowls containing 1.5% agar (E. Merck), as earlier described (Collin et al, 1996). Immobilization is necessary to allow long, continuous recordings of flow in exactly the same tissue volume. With micromanipulators, two laser multireceiver probes (PF 412, Perimed AB, Stockholm, Sweden) were placed approximately 1 mm above an area 5 mm below the cranial pole of each testis in control animals (experiment 1, n = 5 rats) or 1 cm apart on the right testis (experiment 2, n = 7 rats). Large, visible vessels were avoided. The microcirculatory flow was measured by a two-channel laser Doppler flowmeter, PeriFlux PF 4001 Master (Perimed AB, Stockholm, Sweden). The laser Doppler was set to sample a mean of the blood flow 32 times per second. The probes register total erythrocyte flux in a tissue volume of about 2 mm^3 below the thin (50 μm) capsule (Lissbrant and Bergh, 1997). The laser Doppler flow (in arbitrary perfusion units, PU) correlates well with other methods measuring absolute blood flow (Tyml et al, 1990; Turner et al, 1996). Mean systemic blood pressure was measured through a heparinized, saline-filled cannula inserted in the right carotid artery by way of a pressure transducer (SensoNor 840) connected to an isolated pressure amplifier (Lectromed 5290/5291). The laser Doppler and blood pressure signals were transferred on-line to a personal computer and analyzed with the Perimed software Perisoft, version 5.10. A stable blood flow signal with regular vasomotion was recorded for 5 minutes before experiments. After that, blood flow and blood pressure were recorded for 40–53 minutes in each animal.

Table 1. *Average local testicular blood flow at two sites during 40 53-minute registration period**

Experiment	Blood pressure (mmHg)	Blood flow (PU)	Vasomotion	
			Frequency (cycles/min)	Amplitude (PFU)
1†	121 ± −18	243 ± 72	6.5 ± 1.8	164 ± 25
2‡	115 ± 27	224 ± 78	5.3 ± 1.4	157 ± 92

* Values are means ± SD.
† Probes were injected into the left and right testes; n = 5.
‡ Two probes were injected into the same testis; n = 7.

Calculations and Statistics

Values are expressed as means ± SD. Comparisons between groups were made by the Mann-Whitney U-test and by Wilcoxon's test for paired samples. Using Perisoft, the average blood pressure, blood flow, vasomotion frequency, and vasomotion amplitude were calculated for each minute during the observation period. Variability in the studied factors during the study period was described by calculating the minimal value divided by the mean and the maximal value by the mean and by the coefficient of variation (SD/mean). In order to analyze the relative changes in flow parameters in different animals, the recorded values were normalized. The Spearman rank-correlation coefficients (r_s) between the different flow parameters in the two recording probes and blood pressure were calculated. A P value of less than 0.05 was considered significant.

Results

Temporal Variations in Testicular Microcirculation

Variations From Second to Second—Local testicular blood flow was studied in a tissue volume of about 2 mm^3 with a laser Doppler. In this tissue volume, testicular blood flow in our experimental setting is characterized by a regular vasomotion with an average frequency of 5–6 cycles per minute (Table 1). The vasomotion amplitude is high; for example, in experiment 2, the average amplitude is 73 ± 32% of the mean flow (Table 1; Fig. 1). In other words, there are about 5–6 cycles/minute with approximately twofold variations in flow during each minute (Table 1). These rapid temporal variations in flow were generally not correlated at two recording sites in the same testis, suggesting that they are induced by highly local factors and were not correlated to changes in mean systemic blood pressure (mean systemic blood pressure is almost constant during a 1-minute observation period, Fig. 1).

Variations From Minute to Minute—Apart from the above-described large and rapid fluctuations in blood flow, there are also variations with lower frequencies (superimposed over the earlier-described pattern) in intervals of every 5 to 10 minutes. During an observation period of 40–53 minutes, there were several increases and de-

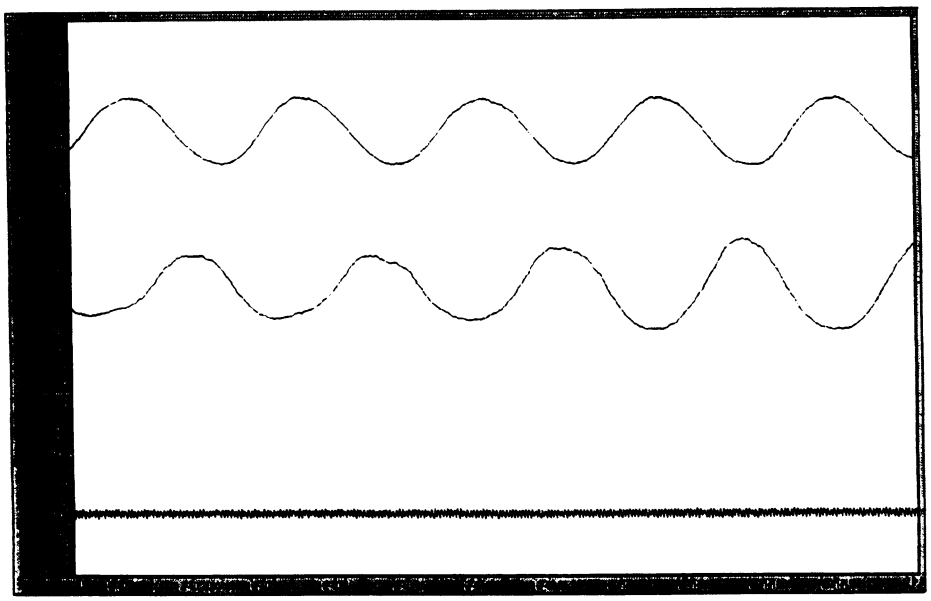

FIG. 1. Laser Doppler flow registration (in perfusion units) with 2 probes (top and middle) at the same testis and mean systemic blood pressure (mm Hg; bottom), during approximately 60 seconds of a 35-minute observation. Time is on the x-axis (hour, minute, and second). This shows a constant blood pressure and that the temporal variations in two different recording sites at the same testis were not correlated to each other. The figure only shows approximately 60 seconds of the experiment, and what in the figure could appear as a negative correlation later on can be seen as a positive correlation; that is, no correlation between the two sites could be observed.

creases in blood pressure, blood flow, vasomotion frequency, and vasomotion amplitude (Table 2). These changes were apparently irregular, unlike the pattern that varied within a minute, and it was not possible to calculate a regular frequency (Fig. 2). The general trend during the observation period was a 25% increase (value at first minute compared with value at last minute) in flow, a 2% decrease in mean blood pressure, a 40% increase in vasomotion amplitude, and an 11% decrease in vasomotion frequency (experiment 2). Because of large intertesticular differences, none of these changes were statistically significant. These temporal variations were analyzed by calculating the average blood flow, vasomotion frequency, vasomotion amplitude, and mean blood pressure for each consecutive minute during 40-minute to 53-minute recordings (experiments 1 and 2). The coefficient of variation (SD/mean) for blood flow, mean blood pressure, vasomotion frequency, and vasomotion amplitude were 0.11, 0.14, 0.23, and 0.36, respectively (experiment 2). The highest variability was seen in vasomotion amplitude, and the lowest variability was seen in blood flow. The variability in flow was, however, not negligible. The minimal and maximal flows divided by the mean flow during the recording period were 0.80 and 1.24, respectively (Table 2). This means that at 40 and 53 minutes, flow change of up to 50% occurred. Correspondingly, vasomotion frequency and vasomotion amplitude show, respectively, fourfold and eightfold changes during the observation period (Table 2).

Table 2. *Minute-to-minute variability in testicular microcirculation during 40–53-minute registration period**

Variable	Minimum/mean	Maximum/mean	SD/mean
Blood pressure	0.80 ± 0.09	1.27 ± 0.1	0.14 ± 0.09
Blood flow	0.80 ± 0.12	1.24 ± 0.16	0.11 ± 0.05
Vasomotion frequency	0.37 ± 0.31	1.45 ± 0.30	0.23 ± 0.10
Vasomotion amplitude	0.22 ± 0.19	1.72 ± 0.26	0.36 ± 0.09

* Results are from experiment 2, in which two probes were injected into the same testis; $n = 7$. Values are means ± SD.

Temporal Changes in Testicular Microcirculation

In order to elucidate factors (systemic vs. local) involved in these temporal variations in testicular blood flow, we analyzed the correlation between two simultaneous flow recordings on the same testis or between the left and right testes.

Experiment With Two Recording Sites on the Same Testis—For the whole group, blood flow, vasomotion frequency, and vasomotion amplitude in the two registration points were correlated, and the Spearman rank coefficients were 0.39, 0.82, and 0.64, respectively ($P < 0.001$, Table 3). Blood flow, vasomotion frequency, and vasomotion amplitude at the two registration points were all correlated to mean systemic blood pressure: $r_s = 0.41$, 0.61, and 0.32, respectively ($P < 0.001$, Table 3). When examining flow parameters in individual testes, there are, however, clear exceptions from the general picture. For example, flow was not correlated in the two registration

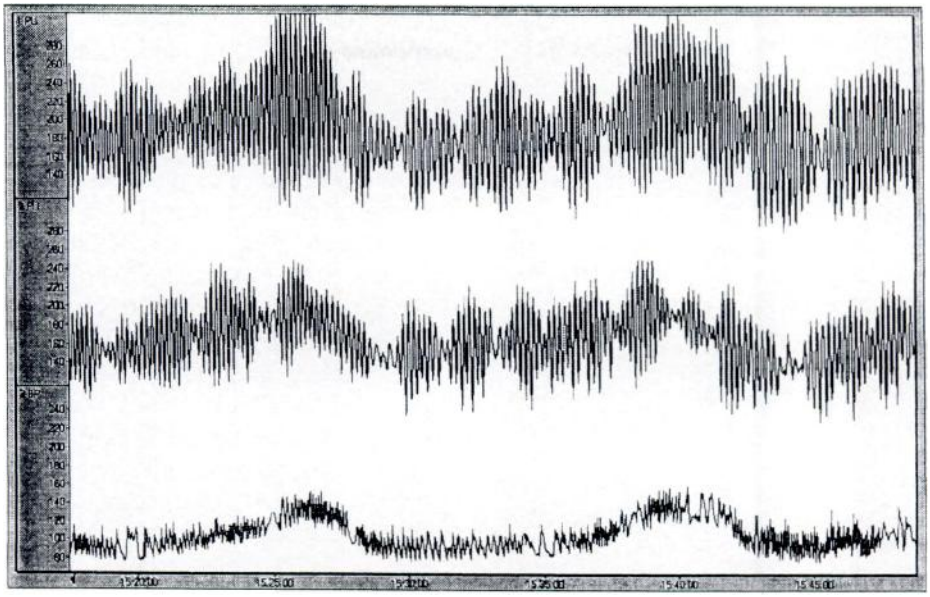

FIG. 2. Laser Doppler flow measurements (in perfusion units) with one probe (top) on the left testis and one probe (middle) on the right testis and blood pressure (mm Hg; bottom) during approximately 35 minutes. Time measurements are on the x-axis (hour, minute, and second). This shows the correlation between blood flow and systemic blood pressure.

points in one animal (animal number 7, Table 3), and flow or vasomotion was not correlated to mean blood pressure in some testes (Table 3). Average flow during the recording period was often different at the two recording sites (spatial variability). The degree of correlation between two recording sites or the degree of correlation between flow parameters and blood pressure was apparently unrelated to average flow.

Table 3. *Spearman rank correlation coefficients ($P < 0.01$) between a variety of variables assessed at two recording sites, a and b, on the same testis during a 40- and 53-minute observation period in anesthetized rats*

Variable	Rat no.						
	1	2	3	4	5	6	7
Flow							
Probe a vs. probe b	0.62	0.92	0.79	0.73	0.49	0.50	NS*
Probe a vs. blood pressure	0.73	−0.50	0.81	0.72	0.45	NS	0.39
Probe b vs. blood pressure	0.40	−0.46	0.69	0.77	NS	0.53	NS
Vasomotion frequency							
Probe a vs. probe b	0.69	NS	0.68	0.64	0.50	0.85	0.76
Probe a vs. blood pressure	0.79	NS	0.65	0.57	0.64	0.76	0.66
Probe b vs. blood pressure	0.84	NS	0.72	0.53	NS	0.82	0.54
Vasomotion amplitude							
Probe a vs. probe b	0.60	0.58	NS	0.66	0.46	0.38	0.33
Probe a vs. blood pressure	0.53	−0.40	NS	NS	−0.36	NS	0.43
Probe b vs. blood pressure	0.53	−0.46	0.76	0.77	−0.37	NS	0.42
Observation time (minutes)	40	51	53	51	51	50	48
Variability during registration period							
Blood pressure	0.16	0.05	0.08	0.29	0.20	0.14	0.06
Blood flow, probe a	0.05	0.09	0.09	0.06	0.15	0.12	0.02
Blood flow, probe b	0.08	0.19	0.08	0.23	0.23	0.08	0.07
Vasomotion frequency, probe a	0.28	0.12	0.23	0.12	0.15	0.25	0.40
Vasomotion frequency, probe b	0.35	0.14	0.20	0.12	0.25	0.23	0.39
Vasomotion amplitude, probe a	0.51	0.33	0.33	0.21	0.33	0.27	0.25
Vasomotion amplitude, probe b	0.56	0.41	0.31	0.16	0.51	0.28	0.28

* NS indicates not significant.

Table 4. *Spearman rank correlation coefficients (P < 0.01) between a variety of variables assessed at recording sites on the left and right testes during a 40- and 53-minute observation period in anesthetized rats*

Variable	Rat no. 1	2	3	4	5
Blood flow					
Probe a vs. probe b	0.86	0.89	0.36	NS*	NS
Probe a vs. blood pressure	0.25	0.68	0.38	0.83	0.70
Probe b vs. blood pressure	0.46	0.55	0.55	NS	NS
Vasomotion frequency					
Probe a vs. probe b	0.52	0.74	0.67	0.91	0.65
Probe a vs. blood pressure	NS	0.68	0.82	0.80	0.30
Probe b vs. blood pressure	NS	0.61	0.69	0.79	0.36
Vasomotion amplitude					
Probe a vs. probe b	0.61	0.18	0.42	NS	0.18
Probe a vs. blood pressure	0.39	NS	0.71	NS	0.37
Probe b vs. blood pressure	0.44	NS	NS	NS	NS
Observation time (minutes)	40	40	40	45	50
Blood pressure (coefficient of variation)	0.14	0.14	0.10	0.11	0.05

* NS indicates not significant.

Experimentation With Recording Sites on the Right and Left Testis—blood flow, vasomotion frequency, and vasomotion amplitude were correlated in the two testes, and the corresponding correlation coefficients were $r_s = 0.58$, $r_s = 0.60$ and $r_s = 0.30$, respectively ($P < 0.001$, Table 4). Blood flow and vasomotion frequency were correlated to mean systemic blood pressure: $r_s = 0.54$, 0.45, and 0.60, respectively ($P < 0.001$, Table 4; Fig. 2). In contrast, vasomotion amplitude was not correlated to mean blood pressure in this experiment. Also in this experiment, individual testes showed a different picture than the majority. For example, flow was not correlated in the two testes in two animals, probably because flow in one of the testes was unrelated to mean blood pressure (rat numbers 4 and 5 in Table 4).

Discussion

This study demonstrates large temporal variations in local intratesticular blood flow in the anesthetized rat. In a tissue volume of about 2 mm^3, there are, within each minute, as a result of a very prominent vasomotion, 5–6 cycles with about twofold changes in blood flow. In addition to this, there are also more slowly occurring variations. Within an observation period of 40–53 minutes, the average blood flow, vasomotion frequency, and vasomotion amplitude for each consecutive minute show substantial variations. For example, the maximal blood flow during this time span is about 1.5-fold higher than the minimal. For vasomotion frequency and amplitude, the maximal amounts were fourfold and eightfold higher than the minimum amounts, respectively. This variability raises two principal questions: 1) what is the functional role (if any) of these variations and 2) how are these variations induced/regulated? The differences in frequency and amplitude in this paper when compared with earlier papers are probably explained by the long time (almost an hour) that the testis was exposed. In unpublicized results, we have noticed that the frequency is reduced and the amplitude increased when there is lengthy exposure. The reason for this is not explained.

Testicular microcirculation is unique in several aspects (Damber and Bergh, 1992; Bergh and Damber, 1993, for review). Capillary pressure, for example, is probably lower than that in all other organs (Sweeney et al, 1991). In all species studied so far (rat, mouse, opossum, ram, and human), local testicular blood flow is characterized by large, rapid, and regular variations (vasomotion; Bergh and Damber, 1993; Collin, 1996; Bergh and Collin, personal observations). The factors influencing testicular vasomotion amplitude and frequency are largely unknown, but the present study suggests that highly local factors are involved (see below). Vasomotion is observed in several other organs but nowhere with such a large amplitude as in the testis. The average amplitude was found in this study to be 73% of the mean, and to our knowledge, there is no tissue in which the amplitude exceeds 20% (Tenland et al, 1983; Allegra et al, 1993). Testicular vasomotion is apparently caused by spontaneous rhythmic myogenic activity in small intratesticular arterioles (Damber et al, 1986). This results in synchronization of capillary blood flow in the tissue volume supplied by a particular arteriole. When such capillary beds are studied by intravital microscopy, periods of rapid flow and periods of completely stopped flow are observed (Damber et al, 1986). This high degree of synchronization and marked variation in erythrocyte velocity probably explains the high vasomotion amplitude observed by the laser Doppler. Several observations indicate that vasomotion is of importance for testicular function. The hematocrit in single microvessels changes in phase with vasomotion, suggesting periodic movement of fluid in and out from testicular microvessels (Damber et al, 1986). Testicular microvessels are highly permeable for macromolecules (Bergh and Damber, 1993; Setchell et al, 1994 for reviews). In the absence of an oncotic pressure gradient between blood and interstitium, it is likely that the periods with slow or no flow (phase with the lowest intravascular pressure) are essential to provide conditions necessary for fluid resorption at the venous side of the microcirculation (Bergh and Damber, 1993). The observation that vasomotion improves tissue oxygenation in other tissues (Intaglietta, 1991) may be of particular importance in the testis because the oxygen ten-

sion in this tissue is remarkably low (Setchell et al, 1994). Given the high vascular permeability in the testis, which makes transvascular fluid exchange critically dependent on fluctuations in local intravascular pressure (Sweeney et al, 1991), it is probably rational to have a regular, large-amplitude vasomotion in this organ. We therefore propose that the rapid and large temporal variations (from second to second) in local testicular perfusion could be a necessary adaptation to a condition with low intravascular pressure and high permeability (all in the end consequences of the scrotal position of the testis; see Bergh and Damber, 1993 for discussion).

The minute-to-minute variations in local blood flow, vasomotion frequency, and vasomotion amplitude were correlated in the right and left testis and in two recording sites on the same testis. The respective correlation coefficients were 0.58–0.39 (blood flow), 0.75–0.82 (vasomotion frequency), and 0.57–0.64 (vasomotion amplitude). This roughly suggests that about 60–85% of the minute-to-minute variability in local blood flow and vasomotion amplitude is caused by some highly local factor and that about 15–40% of the variability is caused by systemic factors influencing all testicular tissue in the same way. For vasomotion frequency, however, it appears that the systemic influence could be slightly larger than the local. Theoretically, the systemic factors synchronizing testicular microcirculation could be blood pressure, neuronal or hormonal influences, changes in blood gases, or temperature. The present study suggests that variation in systemic blood pressure is one important factor. The strongest correlation between systemic blood pressure and testicular microcirculation was for vasomotion frequency (r_s = 0.60–0.61, in the two experiments, respectively), whereas the correlation coefficients for flow (r_s = 0.41–0.54) and vasomotion amplitude (r_s = 0–0.32) were lower. Correlation coefficients of this magnitude indicate that about 36% of the variability in vasomotion frequency, about 16–29% of the variability in flow, and 0–10% of the variability in vasomotion amplitude can be explained by changes in systemic blood pressure. However, the observation that local testicular blood flow is influenced by changes in systemic blood pressure is important. It demonstrates that systemic blood pressure must be continuously measured in studies on testicular blood flow. It also suggest that decreases in blood pressure could reduce testicular blood flow to levels causing tubule damage.

Systemic blood pressure is obviously not the only systemic factor that may influence testicular microcirculation. Synchronization between the vasculature on the right and left side of the body has previously been observed in cutaneous microcirculation and in arterial vasomotion (Schechner and Braverman, 1992; Porret et al, 1995), and autonomic innervation was suggested to be the coordinator. Several studies have shown that the main testicular artery, but not the testicular microvessels, are innervated (Setchell et al, 1994 for review). Theoretically, neuronal influences could therefore be responsible for part of the synchronization between testes. Vasomotion, however, is induced by changes in the diameter of small intratesticular arteries (Damber et al, 1986), in other words, in vessels that lack innervation; it is therefore unlikely that changes in vasomotion are related to temporal changes in neuronal activity. Other systemic factors that could influence both testes are temporal changes in blood gas concentrations, as moderate hypoxia has been demonstrated to reduce testicular blood flow and vasomotion amplitude (Collin, personal observation). Changes in testicular temperature have a pronounced effect on vasomotion amplitude but leave the average flow unaffected (Setchell et al, 1995). In this experiment, temperature was held constant, suggesting that the temporal changes observed in this experiment are not caused by changes in testis temperature. Temporal changes in the systemic hormonal stimulation could also synchronize the testes. If so, however, this does probably not involve the LH–Leydig cell axis, as low doses of LH or endogenous LH pulses do not have any apparent acute effects on testicular microcirculation (Bergh and Damber, 1993; Setchell et al, 1994).

In the present study, we demonstrate that more than 50% of the minute-to-minute temporal variability in flow and vasomotion amplitude (see above) must be related to highly local factors, but the nature of these factors remains unknown. It is generally assumed that metabolism drives local tissue blood flow and that temporal variations in flow reflect temporal changes in local metabolism. Temporal variations in blood flow are a general phenomena. The coefficient of variation for minute-to-minute temporal variations in flow is, for example, 0.23 and 0.25 in normal human skin and in exercising dog muscle, respectively (Tenland et al, 1983; Piiper et al, 1989). In this study, it was 0.11 in the rat testis, but the coefficients of variation for vasomotion frequency and vasomotion amplitude were considerably larger. Hypothetically, the observed temporal variability in testicular microcirculation may suggest that spermatogenesis or some other testicular function could have minute-to-minute variations in its metabolic needs. Whether this is actually the case is unknown. The seminiferous tubules are the most likely candidates for temporal variations in their metabolic demands. The observation that some tubule stages are more sensitive to short-term disturbances in blood flow than others (1 hour of testicular torsion; see Turner et al, 1997) indirectly suggests that different phases of the spermatogenic cycle may have different metabolic demands. The transition from one stage to another, however, takes several hours, and there are as yet no indications of more rapidly occurring variations in seminiferous tubule metabolism. Contractions of the rat testicular capsule and particularly of individual seminiferous tubules (5–6 cycles/minute, Ellis et

al, 1981), however, occur at about the same frequency as testicular vasomotion. Such contractions may influence the local interstitial pressure, and it is possible that they are from time to time more or less in phase with vasomotion. Whether such a mechanism could contribute to the marked temporal variability in vasomotion amplitude remains unknown. An interesting issue to be explored is to what extent interactions between these three factors, influencing interstitial and intravascular pressures, can affect local transvascular fluid exchange in the testis.

In summary, the blood flow in a small testicular volume shows considerable temporal variations. Flow changes from second to second, and the average flow changes from minute to minute. The important question of whether the average flow also shows variations from hour to hour was not studied in the present paper. The second-to-second variations in flow are clearly induced by highly local but at present unidentified factors. The variations that occur within an hour are apparently caused both by systemic factors such as changes in blood pressure and by highly local intratesticular factors. This is not surprising; local tissue blood flow is in general the result of overlapping control systems operating at different levels, such that systemic influences may dominate at some times and local influences may dominate at other times or under particular situations. Such a model of control for local testicular blood flow may also explain variability among individual testes. In some rats, flow was highly correlated in both testes and to blood pressure (dominant systemic control), whereas in other rats' testes, there was no synchronization at all between different parts of the same testis (dominant local control).

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