1 To whom reprint requests should be addressed.
2 We are indebted to Dr. A.F. Pestana de Castro for his suggestions.
3 G.F. Mitchell, Immunology *38*, 209 (1979).
4 H.A. Takehara and I. Mota, Int. Congr. Chagas' Disease 1979, abstracts.
5 D.B. Budzko, M.C. Pizzimenti and F. Kierszenbaum, Infect. Immun. *11*, 86 (1975).
6 F. Kierszenbaum, J. Ivanyi and D.B. Budzko, Immunology *30*, 1 (1976).
7 E.L. Robertson and W.L. Hanson, R. Soc. trop. Med. Hyg. *68*, 338 (1974).
8 R.E. Kuhn and S.K. Durum, Int. J. Parasit. *5*, 241 (1975).
9 D.E. Burgess and W.L. Hanson, Infect. Immun. *25*, 838 (1979).
10 F. Kierszenbaum and M.M. Pinkowski, Infect. Immun. *24*, 117 (1979).
11 Z. Brener, in: Doença de Chagas, p.501. Ed. R. Cançado. Imprensa Oficial do Estado de Minas Gerais, Belo Horizonte 1968.
12 A.C. Corsini, O.L.P. Oliveira and M.G. Costa, Z. Parasitenkd. *61*, 179 (1980).
13 G.G.B. Klaus and J.H. Humphrey, Immunology *33*, 31 (1977).
14 M.H. Julius, E. Simpson and L.A. Herzenberg, Eur. J. Immun. *3*, 645 (1973).
15 A.C. Corsini, O.L.P. Oliveira and M.G. Costa, Z. Parasitkde. *64*, 85 (1980).
16 E.L. Robertson, W.L. Hanson and W.L. Chapman, Exp. Parasitol. *34*, 168 (1973).
17 S.G. Reed, Infect. Immun. *28*, 404 (1980).
18 R. Hoff, J. exp. Med. *142*, 299 (1975).
19 C.J. Sanderson, A.F. Lopez and M.M. Bunn Moreno, Nature *268*, 340 (1977).
20 N. Nogueira and Z. Cohn, J. exp. Med. *148*, 288 (1978).

The negative correlation between erythrocyte concentration and mean corpuscular haemoglobin or mean corpuscular volume in normal dogs

J. Berger

Laboratory of Haematology, Research Institute for Pharmacy and Biochemistry, CS-53351 Pardubice-Rosice (Czechoslovakia), 15 August 1980

Summary. In normal adult Beagle dogs red cell concentration decreased linearly with increasing mean red cell volume and mean red cell haemoglobin. The results are statistically significant ($p < 0.001$).

In toxicological studies performed on Beagle dogs we have observed, in intact animals, negative coefficients of correlation between red blood cell counts (RBCC) and mean corpuscular haemoglobin (MCH) or between RBCC and mean corpuscular volume (MCV). We have found no report on such a relationship of RBCC and MCH or MCV of dogs in the literature. The observed relationships have a bearing on studies of erythropoiesis, clinical interpretation of laboratory data etc., as laboratory dogs are frequently used as a model in biological and medical experiments.

Material and methods. Adult Beagle dogs at the age of 9–49 months (201 males and 197 females) were studied. They were kept individually in air-conditioned indoor dog cages, 0.9×1.0 m. A dry dog diet in pellet form without supplemental vitamins, was supplied at the rate of 0.33 kg/day per animal; water was available ad libitum. The lights were automatically controlled on a 12-h on, 12-h off cycle. Blood samples were taken from the vena cephalica antebrachii 1–3 h after the lights were switched on. Each dog was examined once only. Erythrocyte counts were determined electronically on Celloscope 101 and Picoscale PS-4 counters, haemoglobin on Linson Photometer (540 nm), haematocrit by a micromethod in capillary tubes[1]. All devices were calibrated. MCV was computed from haematocrit and RBCC, MCH from haemoglobin level and RBCC (using Hewlett Packard 1000/40 computer). A least-squares fit was used to determine the slope and intercept for a linear relation[2].

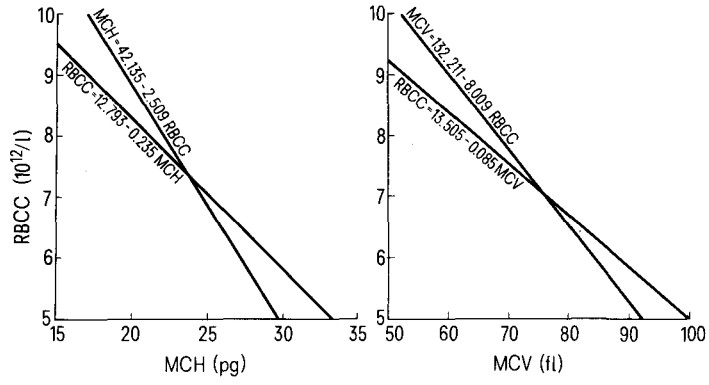
Results. The results are shown in the table. Negative values of correlation coefficients between RBCC and MCH or MCV were obtained. These coefficients of correlation were significant ($p < 0.001$). No significant differences between correlation coefficients for males and females were revealed ($p = 0.38$ for $r_{MCH,RBCC}$, $p = 0.41$ for $r_{MCV,RBCC}$). Therefore, data obtained in males and females were subsequently analyzed together and the results of linear regression analysis are shown in the figure. 2 regression lines are in each part of the figure. One shows the dependence of RBCC on MCH or on MCV (RBCC is on the left-hand side of the equations), the other shows the dependence of MCH or MCV on RBCC (MCH and MCV are on the left-hand side in the equations). As values of correlation coefficients between RBCC and MCH or MCV are similar, the statistical significance of the correlation difference between RBCC and MCV or MCH respectively is for $p = 0.024$; we also computed the coefficient of correlation between MCV and MCH (table); MCV correlates with MCH.

At the same time we computed variation coefficients for the characteristics concerned in males (V_M) and females (V_F) and we found a lower constancy of MCV ($V_M = 14.0$, $V_F = 14.2\%$), MCH ($V_M = 15.1$, $V_F = 14.4\%$) and RBCC ($V_M = 14.1$, $V_F = 15.7\%$) than MCHC ($V_M = 9.8$, $V_F = 7.4\%$),

Coefficients of correlation (r) between values of red blood cell concentration (RBCC) and mean corpuscular haemoglobin (MCH) or between RBCC and mean corpuscular volume (MCV)

Characteristic	Males	Females	Males and females
RBCC ($10^{12}/l$)	7.03 ± 0.07[a]	7.12 ± 0.08	7.07 ± 0.05
MCH (pg)	24.53 ± 0.26	24.25 ± 0.25	24.39 ± 0.18
MCV (fl)	75.88 ± 0.75	75.23 ± 0.76	75.56 ± 0.53
$r_{MCH,RBCC}$	−0.741	−0.793	−0.767
$p(r_{MCH,RBCC})$	<0.001	<0.001	<0.001
$r_{MCV,RBCC}$	−0.806	−0.845	−0.826
$p(r_{MCV,RBCC})$	<0.001	<0.001	<0.001
$r_{MCV,MCH}$			+0.791
$p(r_{MCV,MCH})$			<0.001
number of animals	201	197	398

[a] Means ± SEM. $p(r_{MCH,RBCC})$, $p(r_{MCV,RBCC})$ and $p(r_{MCV,MCH})$ are levels of statistical significance of the correlation coefficients concerned.



Graph of the regression lines for laboratory dogs showing the linear relation of mean cell haemoglobin (MCH) and red blood cell counts (RBCC) or the linear relation of mean corpuscular volume (MCV) and RBCC.

haemoglobin concentration ($V_M = 10.7$, $V_F = 8.8\%$) and haematocrit ($V_M = V_F = 7.7\%$). These data suggest that correlations among MCV, RBCC and MCV, which are computed above, might be decisive in the controlling mechanism in the red blood picture of normal adult dogs.

Discussion. We have found no report on a negative coefficient of correlation between MCH and RBCC in any animal species or in human subjects. There is one report of such a relationship between human MCV and RBCC[3] but no report for other species has been found. The MCH values depend upon the haemoglobin synthesis and the cell volume (MCH = MCHC × MCV). As the MCHC is relatively constant (cf. variation coefficients), the basic relationship is between MCH and MCV. Thus, the erythrocyte volume might be important in the controlling mechanism. Nevertheless, the MCV depends upon haematocrit and RBCC (MCV = haematocrit/RBCC). As both haematocrit and haemoglobin levels are relatively constant (cf. variation coefficients), both MCV and MCH seem to be decisive in controlling the mechanisms of RBCC, which we confirmed by the higher statistical significance of correlation between RBCC and MCV or MCH as well. Our findings partially explain clinical experience that RBCC are usually a less responsive determination than other characteristics made in the examination of the red blood picture, particularly haematocrit[4] and MCHC[5].

1 J. Berger, Zwierz. lab. *17*, 17 (1980).
2 H. Grimm, in: Biostatistics in Pharmacology, p. 717 and p. 739. Ed. A.L. Delanois. Pergamon Press, Oxford 1973.
3 R.E. Lovlin, L.S. Sewchand, J.S. Beck, and S. Rowland, Blut *38*, 361 (1979).
4 A.C. Andersen and O.W. Schalm, in: The Beagle as an Experimental Dog, p. 261. Ed. A.C. Andersen. Iowa State University Press, Ames, Iowa 1970.
5 O.W. Schalm, Veterinary Hematology. Lea and Febiger, Philadelphia 1961.

Hypothalamus-adenohypophysis-thyroid axis in spontaneously hypertensive rats (SHR)

P.T. Männistö and J. Mattila

Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10A, SF-00170 Helsinki 17 (Finland), 5 August 1980

Summary. Increased basal TSH levels and an enhanced response to cold-exposure were apparent in the SHR accustomed to +30 °C, whereas goitres and an increased amount of the anterior pituitary TSH were measured in SHR kept at +20 °C.

Spontaneously hypertensive rats (SHR) which were originally isolated by Okamoto and Aoki[2], have been widely used as an animal model for essential hypertension. From the very beginning small but definitive abnormalities were observed in the endocrine function of SHR[3], e.g. basal TSH levels were somewhat higher in SHR than in the various control rats[4-7]. In 1 study[6], the TSH-response to exogenous TRH was enhanced in SHR. Furthermore, SHR have had small goitres[2,4,5] or an increased uptake of radioiodine[2,4]. Although there has not been very marked hypertrophy of the anterior pituitaries in SHR[2,3], basophilic[3] or more specifically thyrotrophic cells[8] have been relatively increased. The levels of serum thyroid hormones have sometimes been low[4,5,9]. These data from several sources have not been easy to interpret, and definitive conclusions about the level of the disturbance have not been drawn.

We have now compared the dynamics of the hypothalamus-anterior pituitary-thyroid gland axis in the SHR and the Wistar-Kyoto (WKY) control rats, trying to localize the possible error of this axis. We have measured hypothalamic TRH levels, anterior pituitary TSH concentrations and serum TSH and thyroid hormone levels both under basal conditions and during cold- and TRH-stimulation.

Materials and methods. SHR and WKY control rats were originally obtained from NIH and then inbred in our department. The rats were used at the age of about 8 months. They were fed with common laboratory pellets (iodine content 0.5-1 mg/kg) and tap water ad libitum. Blood pressure of SHR was between 150 and 210 mmHg and that of WKY rats between 100 and 135 mmHg, when measured about 2 weeks before the experiments. Some of the rats were adapted to +30 °C for 7 days before use. The cold-exposure was used to elevate serum TSH levels (+4 °C for 30 min). The TSH cold-response is known to be mediated via increased TRH-release in the hypothalamus[10,11], and this test is therefore used to study changes in the activity of the hypotalamic TRH neurons. The warmth-adaptation has been a routine because a high cold-response