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IMMUNE-RELATED HEALTH-RELEVANT CHANGES IN NATURAL POPULATIONS OF NORWAY RAT (*RATTUS NORVEGICUS* BERKENHOUT, 1769): WHITE BLOOD CELL COUNTS, LEUKOCYTE ACTIVITY, AND PERIPHERAL ORGAN INFILTRATION

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Abstract — Basic immune-related health-relevant changes (total and differential white blood cell counts and activity, leukocyte tissue infiltration, and related pathohistology) were assessed in wild Norway rats from urban habitats. Comparative measurements were conducted in individuals of several laboratory strains of Norway rat in order to gain insight into environmental effects on the health of wild rats. Changes in leukocyte counts and activity along with tissue infiltration were noted only in wild rats, indicating systemic as well as tissue inflammation in these animals. Coincidence of these changes with chronic inflammatory pulmonary and kidney disease was observed in the majority of affected rats.

Key words: Wild Norway rats, leukocytes, tissue inflammation

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INTRODUCTION

Norway rat (*Rattus norvegicus* Berkenhout, 1769) is a common rodent species with wide distribution, mostly in urban and suburban habitats. It is a eusynanthropic animal, living near humans, who provide it with food and shelter. Due to their significance for human well-being, Norway rats have been the subject of numerous studies as they cause economic losses, as carriers of various zoonotic pathogens relevant for public health (Kataranovski et al., 1995, 1997; Bradshaw, 1999; Battersby et al., 2002; Klein et al., 2002; Easterbrook, 2007), or as indicators of an environmental pollution hazard (Fouchecourt and Riviere, 1995; Eckle and Riegler, 1997; Ceruti et al., 2002; Doungchawee et al., 2002). One of the major aspects that should be considered in such studies is the use of healthy animals. Although it may be difficult to determine the health of wild rats, evaluation of the state of the immune system, an essential health factor, can offer an important insight into the overall state of health of the animal. In this context, simultaneous examination of rats from natural habitats and individuals of laboratory Norway rat strains that have been raised shielded from a variety of environmental stimuli appears to be a promising way to assess the immune/health status of individuals from natural populations.

The aim of this study was to assess the state of the immune system in wild Norway rats from an urban environment by examining white blood cells from circulation and their presence/engagement in peripheral organ tissue (lungs, liver, and kidneys). Quantitative (cell counts and differentials) and some qualitative (leukocyte capacity to form clusters and superoxide formation activity) parameters were measured, along with histological assessment of leukocyte tissue infiltration and related histopathological changes in peripheral organs. In order to reduce (to some extent) the contribution of variations due to the effect of internal and external

(environmental) factors, individuals of the same age class and of both sexes caught in ecologically similar habitats and during the same seasons were analyzed. Measurements were conducted comparatively in age- and sex-matched individuals of several laboratory strains of Norway rat. The obtained evidence indicated the presence of systemic inflammation in some of the wild Norway rats. Signs of chronic lung inflammatory disease, noted in the majority of these individuals, suggest a relationship between systemic and lung inflammation. The collected data represent an initial source of health-relevant baseline information regarding leukocyte changes in the circulation and tissues of Norway rats from natural populations that might be useful for further studies on this species.

MATERIALS AND METHODS

Animal collection and maintenance

Rats were captured with live traps in the urban area of Belgrade, Serbia (44°N, 20°E, with the approximate geometric center of Belgrade at 44°49'14"N, 20°27'44"E). Animals were collected from March to September in 2005 and 2006 during time periods when deratization had not been carried out and were transported to an appropriate facility of the Siniša Stanković Institute for Biological Research in Belgrade. Upon arrival, they were housed in wire-mesh cages for one week in order to adapt to captivity. Pregnant females and ones that gave birth in the laboratory prior to analysis, as well as animals with external injuries, were not used. Laboratory rats housed at the aforementioned institute were used for comparative evaluation. Individuals of the Wistar, Albino Oxford, and Dark Agouti lines were used to avoid domination of specific characteristics of one particular strain. Animal treatment was carried out in conformity with requirements of the Institute's Ethical Committee. Rats were fed commercial rodent feed and had access to water *ad libitum*. Age class designations were determined from dry eye lens weight as described by Kataranovski et al. (1994). Observation of the clinical status of the animals was done after blood collection on specimens euthanized under anesthesia by cervical dislocation. Clinical examination consisted of morphological observations, including evaluation of body condition and checking for the presence of wounds.

Blood collection

Animals were anesthetized by intraperitoneal (i. p.) injection of thiopental sodium (Rotexmedica, Tritau, Germany). Blood was withdrawn from the abdominal aorta with a syringe and used for determination of white blood cell counts and the state of leukocyte aggregation/adhesion.

Peripheral blood total and differential leukocyte counts

A measured volume (10 μL) of whole blood was diluted in 40 μL of Türk solution, and leukocytes were counted using an improved Neubauer hemocytometer chamber. Leukocyte differential counts were performed by differentiating at least 300 cells from air-dried whole blood smears stained according to the May Grünwald-Giemsa protocol.

Whole blood nitroblue tetrazolium (NBT) reduction assay

Reduction of NBT by neutrophils and monocytes, as a measure of spontaneous cell-derived superoxide formation, e. g., cell activation, was determined in fresh blood according to a modification of the method described by Shen et al. (1995). Briefly, blood was diluted (4 volumes of blood and 1 volume of complete medium) with Roswell Park Memorial Institute (RPMI)-1640 cell culture medium (Flow, ICN Pharmaceuticals, Costa Mesa, USA) supplemented with 2 mM glutamine, 5 x 10^{-5} M 2-mercaptoethanol, 60 μg/ml gentamycin, and 5% (v/v) heat-inactivated fetal calf serum (complete medium). Diluted blood (100 μL) was incubated with 0.5 mg/ml of NBT at 37°C for 20 minutes, followed by 10-min incubation at room temperature. Enumeration of cells with intracellular dots of formazan (NBT-positive cells) was performed by optical microscopy on blood smears stained according to the May Grünwald-Giemsa protocol.

Whole blood assay of peripheral blood leukocyte aggregation/adhesion (LAA)

A direct slide blood test (Berliner and Aronson, 1991) was used to estimate the state of peripheral blood leukocyte aggregability/adhesiveness. Briefly, withdrawn blood was diluted with 3.8% sodium citrate (1 volume of sodium citrate: 4 volumes of blood), and several large blood drops were placed on a slide that was held for 2-3 sec at an angle of 45° (ensuring slipping down of blood by gravity, leaving a fine blood film). Leukocyte aggregability was determined on hematoxylin-eosin–stained slides. Cells were considered aggregated when three or more nuclei were placed less than one cell diameter apart. The percentage of aggregated leukocytes on the slides was determined by counting at least 300 white blood cells. For example, if 9 cells out of 300 are in aggregates, the percentage of aggregated leukocytes is 3.0%, regardless of whether two aggregates of four and five cells or three aggregates of three cells each were noted.

Histology

Lung, liver, or kidney tissue was cut and immediately fixed in 4% formaldehyde (pH 6.9). After processing, tissue was embedded in paraffin wax for sectioning at 5 μm. Hematoxylin and eosin (H&E)-stained histology slides were subsequently analyzed by light microscopy.

Data display and analysis

Results are expressed as means ± SD, with range values for white blood cell counts and acivity evaluations. Data concerning leukocyte aggregability and the presence of disease were expressed as prevalence and percent prevalence of animals. Statistical analyses were performed using the STATISTICA 7.0 statistical software package (StatSoft Inc., Tulsa, Oklahoma, USA). Significance was defined by two-sided difference tests, *P*-values less than 0.05 being considered significant.

RESULTS

General animal population data

A total of 48 wild Norway rats (20 males and 28 females) were selected for the study based on mature age (3-12 months old). Physical examination of the animals gave indication of good body condition and

Table 1. White blood cell counts in Norway rats. Abbreviations: a) mean±SD, b) range (min-max).

	Wild			Laboratory		
Parameter	Males (n = 20)	Females (n = 28)	Combined (n = 48)	Males (n = 27)	Females (n = 21)	Combined (n = 48)
Total	11.9±9.2[a]	9.7±6.1	9.1±6.9	7.2±2.0	4.8±2.1	6.2±2.8
Leukocytes (10^9/L)	(2.8-34.4)[b]	(3.4-25.0)	(1.7-**34.4)**	(3.0-15.7)	(2.0-8.7)	(2.0-15.7)
Lymphocytes (%)	70.2±15.1	76.4±10.1	73.8±12.6	83.3±7.3	84.2±4.8	84.6±7.9
	(38.0-89.0)	(56.8-94.0)	(38.0-94.0)	(63.0-95.3)	(78.0-94.0)	(63.0-95.3)
Neutrophils (%)	23.1±16.1	17.8±8.8	20.0±12.4	14.6±5.5	11.4±6.8	13.2±6.3
	(4.6-57.0)	(3.8-34.0)	(3.8-57)	(4.7-27.0)	(1.7-27.0)	(1.7-27.0)
Monocytes (%)	5.8±4.4	3.9±2.9	4.8±3.6	2.2±2.1	1.6±2.3	1.9±2.2
	(0.3-14.6)	(0.2-14.0)	(0.2-14.6)	(0-5.8)	(0-6.0)	(0-6.0)
Eosinophils (%)	0.7±1.1	1.6±1.8	1.2±1.6	0.4±0.6	0.5±0.8	0.5±0.7
	(0-3.4)	(0-5.8)	(0-5.8)	(0-2.2)	(0-4.0)	(0-4.0)
Basophils (%)	0.2±0.3	0.3±0.4	0.2±0.3	0.05±0.1	0.06±0.1	0.05±0.1
	(0-1.2)	(0-1.2)	(0-1.2)	(0-0.6)	(0-0.7)	(0-0.7)
Neutrophils	0.4±0.4	0.2±0.2	0.3±0.3	0.2±0.1	0.1±0.1	0.1±0.1
Lymphocytes	(0.05-1.5)	(0.04-0.6)	(0.04-1.5)	(0.02-0.4)	(0.02-0.3)	(0.02-0.4)

Table 2. State of peripheral blood leukocyte aggregation/adhesion (LAA) and leukocyte superoxide formation (NBT+) in Norway rats. Abbreviations: a) prevalence of leukocyte aggregability or NBT reduction capacity, b) LAA or NBT value (mean % ± SD), c) % range (min-max), *statisticaly different from laboratory animals at $p < 0.02$.

	Wild			Laboratory		
	Males (n = 20)	Females (n = 28)	Combined (n = 48)	Males (n = 27)	Females (n = 21)	Combined (n = 48)
Leukocyte aggregability						
LAA ≥ 5%	4/20 (20.0%)[a]	6/28 (21.4%)	10/48 (20.8%)*	0/27 (0.0%)	2/21 (9.5%)	2/48 (4.2%)
	10.5±4.6[b]	16.8±7.4	14.3±6.9		7.2±1.7	7.2±1.7
	(5.0-16.0)[c]	(6.0-24.0)	(5.0-24.0)		(6.0-8.4)	(6.0-8.4)
NBT^+ cells						
Neutrophils	11/20 (55.0%)[a]	22/28 (78.5%)	33/48 (68.7%)	20/27 (74.0%)	16/21 (76.0%)	36/48 (75.0%)
	2.4±3.4[b]	2.4±3.4	2.3±3.1	1.5±0.9	2.0±1.7	1.8±1.4
	(0.4-5.3)	(0.2-14.0)	(0.2-14.0)	(0.8-2.6)	(0.7-5.3)	(0.7-5.3)
Monocytes	3/20 (15.0%)	6/28 (21.4%)	9/48 (18.7%)	9/27 (31.3%)	8/21 (38.1%)	17/48 (35.4%)
	3.9±1.1	3.1±1.9	3.2±1.6	4.4±1.7	3.2±0.7	3.8±1.4
	(2.7-4.8)	(1.8-6.0)	(1.8-6.0)	(2.1-8.3)	(2.2-4.0)	(2.1-8.3)

apparent health. Age-matched laboratory animals (27 males and 21 females) were used in the study.

Quantitative peripheral blood leukocyte data

Leukocyte values in the peripheral blood of Norway rats from natural and laboratory populations are shown in Table 1. Wide ranges of total leukocyte and relative neutrophil and monocyte numbers were noted in wild Norway rats. High total numbers of leukocytes (compared to published values as well as the values in this study) noted in two males (33.6 x 10^9/L and 34.4 x 10^9/L) were responsible for the high upper value within the total leukocyte number range in wild *vs.* laboratory rats. In two male wild rats, high relative numbers of neutrophils (50.8 and 57.0%) concomitantly with low numbers of lymphocytes (41.0 and 38.0%) were noted, contributing to a high upper value within the neutrophil range and a low lower value within the lymphocyte range. A wide range of relative numbers of monocytes was noted in wild rats owing to high (compared to published values as well as the values in this study) numbers in male (10.2±2.9%) and (8.3±2.8%) female individuals. Monocyte increase was noted in 8/20 (40%) males and in 4/28 (14.3%) female individuals of wild Norway rats. In one male rat with high leukocyte counts, increased numbers of monocytes were noted as well, and one male had a simultaneous increase in relative numbers of monocytes and neutrophils. Thus, a total of 50.0% (10/20) of males and 14.3% (4/28) of females, e. g., 29.2% of all wild rats that were studied had high total blood leukocyte and/or leukocyte differential counts.

State of blood leukocyte aggregation/adhesion (LAA) and activation status (NBT-reducing capacity)

When white blood cell aggregability (proportion of cells which formed aggregates *in vivo*) was measured, similar numbers of wild rats (31.2%) and laboratory animals (45.8%) without aggregated cells (LAA = 0%) and with low percentages (LAA < 5%) of aggregated cells (47.9 and 50.0%, respectively) were noted. However, significantly higher numbers of individuals with increased aggregability (LAA values ≥ 5%) were noted in wild rats (Table 2). Leukocyte aggregates were composed of neutrophils and mononuclear cells (Fig. 1).

When the activation status (superoxide formation, NBT-reducing capacity) of peripheral blood leukocytes was determined, similar ranges of relative numbers of NBT^+ neutrophils were noted in

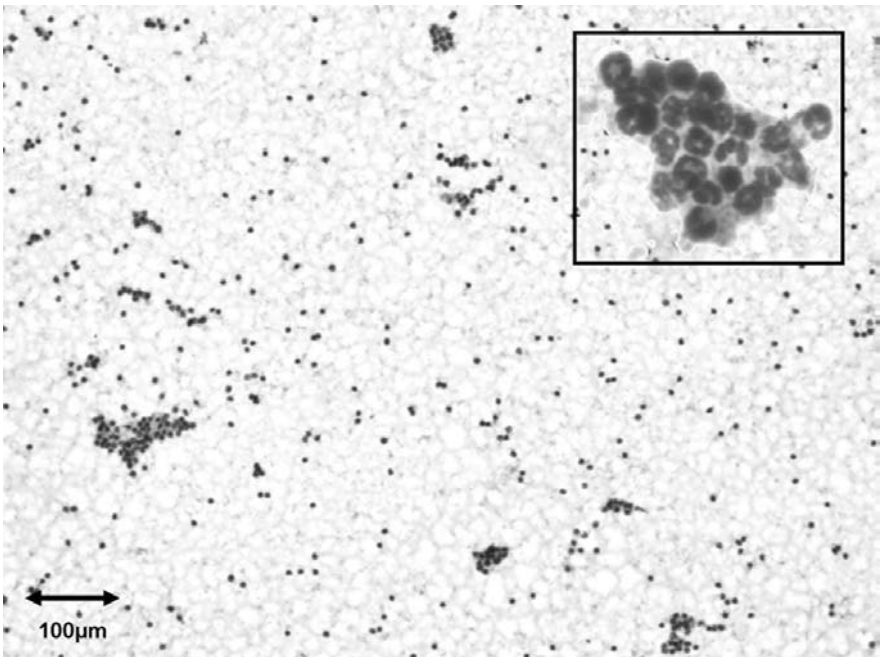

Fig. 1. Peripheral blood leukocyte aggregates in Norway rats from natural populations.

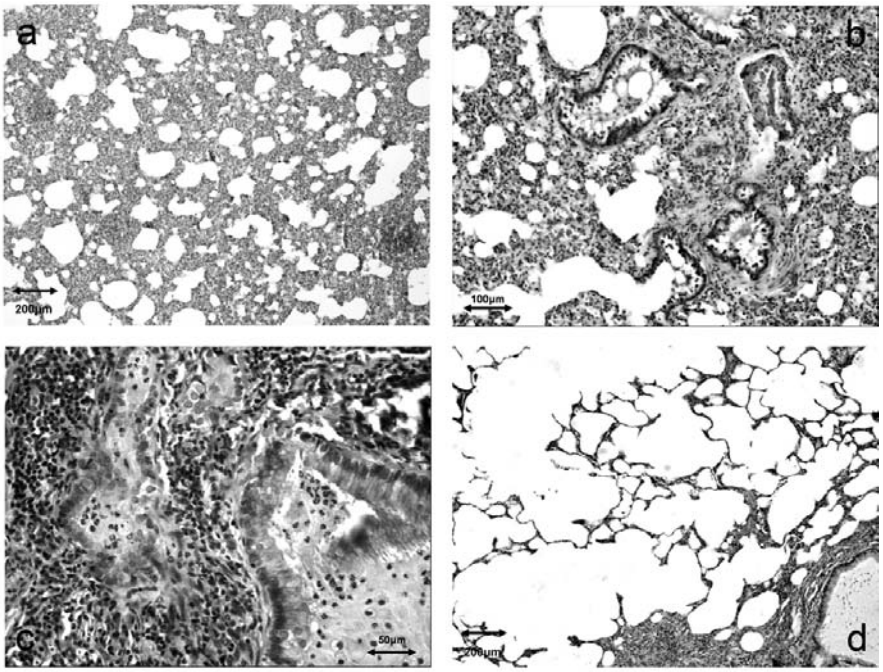

Fig. 2. Pulmonary disease in Norway rats from natural populations. a - inflammation of the alveolar portion of the lung, collapse and consolidation; b - dilated bronchus with hyperplastic and degenerated epithelium, mucus and desquamated epithelial cells in the lumen; inflammatory cells in bronchial wall and thick interstitium; c - bronchiectasis surrounded by rich mixed inflammatory infiltrate; lumen filled with mucus and neutrophils; d - emphysema with dilated bronchus.

Table 3. Prevalence of chronic inflammatory disease and peripheral blood leukocyte changes in wild Norway rats. Abbreviations: a>33 x 109/L, b>50%, c>7%, *p < 0.02 vs. females.

	Lungs			Kidneys		
	Males (n = 20)	Females (n = 28)	Combined (n = 48)	Males (n = 27)	Females (n = 21)	Combined (n = 48)
Affected individuals	9/20 (45.0%)	7/28 (25.0%)	16/48 (33.3%)	4/20 (20.0%)	8/28 (28.6%)	12/48 (25.0%)
Leukocyte changes in affected individuals	9/9 (100.0%)*	3/7 (42.3%)	12/16 (75.0%)	3/4 (75.0%)	4/8 (50.0%)	7/12 (58.3%)
Leukocyte counts in affected individuals						
Total leukocytes[a]	2/9 (22.2%)	0/3 (0.0%)	2/12 (16.7%)	1/3 (33.3%)	0/4 (0.0%)	1/7 (14.3%)
Neutrophils[b]	2/9 (22.2%)	0/3 (0.0%)	2/12 (16.7%)	2/3 (66.7%)	0/4 (0.0%)	2/7 (28.6%)
Monocytes[c]	6/9 (66.7%)	0/3 (0.0%)	6/12 (50.0%)	0/3 (0.0%)	2/4 (50.0%)	2/7 (28.6%)
Leukocyte activity in affected individuals						
LAA (> 5%)	1/9 (11.0%)*	3/3 (100.0%)	4/12 (33.3%)	0/3 (0.0%)	0/4 (0.0%)	0/7 (0.0%)
NBT^+ cells (> 10%)	0/9 (0.0%)	1/3 (33.3%)	1/12 (8.3%)	0/3 (0.0%)	0/4 (0.0%)	0/7 (0.0%)

male individuals of wild and laboratory rats, while a wide range of activated neutrophils was noted in wild female rats (Table 2). High numbers of activated neutrophils (12.5 and 14.0%) noted in two females were responsible for the high upper value within the range of NBT^+ cells in wild female rats and in total animals from urban habitats. In contrast, a low prevalence of NBT^+ monocytes was noted in wild-caught animals.

Lung, kidney, and liver histopathology

To obtain more data on leukocyte changes relevant for health in rats caught in urban habitats, leukocyte infiltration and related histologically evident signs of tissue pathology and disease in vital organs (lungs, kidneys, and liver) were analyzed. Collapse and consolidation of some portions of the lung, bronchial dilatation with hypersecretion and desquamation of bronchial epithelium, emphysema, and bronchiectases were detected, demonstrating severe lung disease in rats from natural populations (Fig. 2). No such changes were noted in the lungs of laboratory rats. Higher prevalence of lung disease was noted in males compared to female individuals of wild rats, although without statistical significance (Table 3). All wild male rats with lung disease had changes in white blood cells as well, while such a coincidence was noted in less than 50.0% of females. High total and differential white blood cell counts were noted in almost all wild male rats with pulmonary disease, while qualitative changes (leukocyte aggregability and superoxide formation) were more prevalent in females.

In the lungs of animals with changes in leukocyte numbers/activity but no signs of severe pulmonary disease (n = 4, males and n = 5, females), signs of inflammatory activity were noted, including interstitial inflammation with leukocyte infiltration and interstitial widening of various intensity, sometimes with reactive changes in blood vessel walls (not shown). In animals without signs of disease and with no changes in peripheral blood leukocytes, discrete peribronchial and perivascular leukocyte infiltration was the sole finding.

Histological examination of kidneys from wild rats revealed signs of chronic inflammation-related kidney disease, including tubulointerstitial disease and chronic pyelitis (Fig. 3). No such changes were noted in laboratory rats. The prevalence of chronic kidney disease in wild rats is shown in Table 3. The majority of male and half of female wild Norway rats with kidney inflammation had changes in white blood cells as well. High numbers of white blood cells were noted in all males with kidney disease. Males with high total white blood cell and neutro-

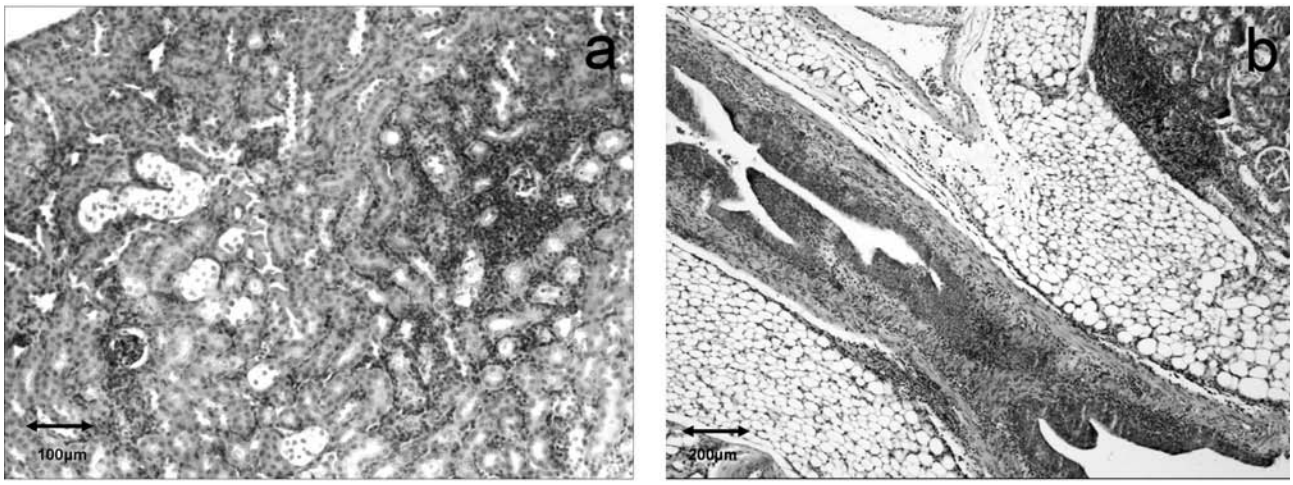

Fig. 3. Kidney inflammation in Norway rats from natural populations. a - tubulointerstitial nephritis; peritubular interstitial mononuclear leukocyte infiltration with tubular dilatation and degeneration; b - chronic pyelitis; diffuse polymorphonuclear inflammatory infiltrate; lymphoid aggregation near renal parenchyma.

phil numbers had lung inflammatory lung disease as well. No changes in peripheral blood leukocytes were noted in females with kidney disease, except for high numbers of monocytes in two females. No signs of chronic pulmonary disease were noted in these individuals.

No signs of inflammation-related chronic liver disease were noted in wild Norway rats.

DISCUSSION

In this study, quantitative and qualitative changes in peripheral blood leukocytes and leukocyte-related histologically evident changes in peripheral organs (lung, liver, and kidney) were determined in Norway rats from natural populations and compared to corresponding values in laboratory rats. Determination of total and differential peripheral blood cell counts is a widely used approach in assessing the state of the immune system in natural populations of vertebrates (Wolk and Kozlowski, 1989; Robel et al., 1996; Weber et al., 2002) and represent an *ex vivo* indirect measure of immune system performance (Owens and Wilson, 1999). In line with data for laboratory Norway rats in this study and the literature data for other Norway rat strains (Mitruka and Rawnsley, 1977; Sharp and Regina, 1998), lymphocytes outnumber neutrophils in the majority of rats from natural populations, with resultant low values of the neutrophil to lymphocyte ratio. High white blood cell counts, a shift in favor of neutrophils, and high relative numbers of monocytes noted in more than 20% of wild rats reflect immune system engagement in these animals. High numbers of peripheral blood leukocytes in some of the wild rats possibly resulted from the need for newly produced cells in these individuals. Their parasite load – including viruses, bacteria, protozoa, and ectoparasites (apart from gastrointestinal helminths) (Battersby et al., 2002; Easterbrook et al., 2007) – might have been responsible for this demand in the rats from urban habitats.

An increase in numbers of circulating leukocytes is a normal physiological response to stimuli of various nature (Schwartz and Weiss, 1991) and is widely considered to be a part of systemic inflammation (Schwartz and Weiss, 1991; Asimakopoulos, 1999). High values of circulating neutrophil leukocytes, cells responsible for the host's initial defense (Nathan, 2006), and monocytes, cells with high potential in tissue inflammation (Gordon and Taylor, 2005), in some of the wild rats might thus be regarded as an indicator of an ongoing inflammatory response in these animals. High monocyte counts indicated chronicity of inflammation, and tissue pathology consistent with persistent inflam-

mation supports this notion.

The state of leukocyte adhesiveness/aggregability (LAA in vivo), the phenomenon of leukergy (Berliner and Aronson, 1991), is a nonspecific indicator of inflammation at the systemic level (Maharshak et al., 2000). Owing to its simplicity, this index is used to screen for the presence of systemic inflammation and measure its intensity in laboratory animals (Fried et al., 1991; Molad et al., 1993) and for assessment of infection in humans (Molad et al., 1993; Vainer et al., 2004). In accordance with these studies, increased relative numbers of peripheral blood leukocytes in aggregates in more than 20% of wild Norway rats suggest a higher incidence of systemic inflammation in rats from natural populations compared to laboratory rats. Increased *in vivo* activity of white blood cells in wild Norway rats might have resulted from plasma inflammatory mediators (inflammagens), as shown in experimental laboratory research (Berliner et al., 1987; Zeltser et al., 1998). Research on plasma mediators involved in systemic inflammation in animals from natural populations warrants future attention.

Although a low average level of spontaneous neutrophil activation was noted in both natural and laboratory rat populations, the numbers of spontaneously activated neutrophils were greater in wild animals with high numbers of leukocytes and neutrophils. Thus, a total of 12.5% of all wild rats examined, 20.0% of males (two individuals with high leukocyte counts and two individuals with high neutrophil counts), and 7.1% of females (two individuals with high percentage of NBT^+ neutrophils) had high numbers of spontaneously activated white blood cells. Given the correlation between the level of spontaneous superoxide production by granulocytes and the magnitude of this response following stimulation in settings of systemic inflammation in laboratory rats (Wikstrom et al., 1996), an increase in numbers of activated neutrophils might be beneficial for the innate immune defense in these animals. However, owing to their ambiguous role in inflamed tissue (protective/successful in elimination of infection, but deleterious when excessively activated) (Nussler et al., 1999), increased numbers of activated blood leukocytes represent a potential risk for peripheral tissues. Coincidence of high numbers of neutrophils with the presence of histologically evident signs of inflammation-related pulmonary disease supports such an assumption.

The chronic lung and kidney disease noted in wild rats is of inflammatory etiology (Brentjens et al., 1982; Fahy et al., 1992; Kodavanti and Costa, 2001), and leukocyte infiltration indicates the significance of inflammatory response for disease establishment/maintainance. A chronic infiltrating inflammatory cell response to microbial colonization in experimental bronchiectasis was shown to be responsible for mucus secretion in rats (Lapa e Silva et al., 1989; Fahy et al., 1992), and a contribution of inflammatory cell-derived proteases and products of oxidative metabolism to tissue damage and its progression to destruction of alveolar septal walls (emphysema) was documented by Kodavanti and Costa (2001). Immune mechanisms were considered as principal in mediating renal damage in laboratory rats (Okada et al., 2000). The observed changes might have mainly resulted from local inflammatory activity, although a contribution of systemic inflammation cannot be ruled out. Coincidence of pulmonary and renal chronic inflammatory disease in some of the wild rats and changes in peripheral blood leukocyte counts/activity in these animals suggest a relationship between systemic (in circulation) and inflammatory changes in the tissues. In connection with this, quantitative and qualitative peripheral blood leukocyte changes might have resulted from the inflammatory activity in the lungs and kidneys (at least in male wild rats). However, by way of analogy with data which demonstrated a relationship between tissue leukocyte infiltration/activation and subsequent organ complications in settings of systemic inflammation (Yao et al., 1998), a contribution of changes in white blood cell counts/activity to the observed local tissue changes might be assumed. In connection with this, increased adhesiveness and aggregation of peripheral blood leukocytes (LAA) and the presence of leukocytes in lungs were noted in settings of tissue injury in laboratory mice (Fried et al., 1991) and in dogs (Molad et al., 1993), leading to a proposal calling for use of LAA values as markers of tissue leukostasis. Data showing the exis-

tence of a correlation of the distribution of activated (NBT^+) granulocytes and circulation and the lungs in settings of systemic inflammation in laboratory rats (Wikstrom et al., 1995) imply a further contribution of increased numbers of activated white blood cells to the development of inflammatory-based pulmonary diseases in wild-caught rats. High numbers of peripheral blood monocytes, precursors of a variety of tissue macrophages with known high potential in local tissue inflammation (Gordon and Taylor, 2005), suggest their involvement in tissue inflammation/damage as well.

In conclusion, the data obtained in this study demonstrate quantitative and qualitative differences in the peripheral blood leukocyte compartment of a substantial proportion of rats from urban habitats. Coincidence of changes in white blood cell counts/properties with inflammation-related pulmonary and kidney disease in the majority of affected individuals suggests a relationship between parameters of the immune system in circulation and peripheral tissues. By determining leukocyte changes in both locations (circulation and tissue), a more integrated view of immune-relevant activity in rats from natural populations might be obtained. The collected data represent an initial source of baseline information about the immune system/health status of Norway rats from natural populations that might be useful for further studies on this species, including studies focused on environmental health and the immunotoxicity of environmentally-relevant chemicals.

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ИМУНОЛОШКЕ ЗДРАВСТВЕНО ЗНАЧАЈНЕ ПРОМЕНЕ КОД СИВОГ ПАЦОВА (RATTUS NORVEGICUS BERKENHOUT, 1769): БРОЈ И АКТИВНОСТ ЛЕУКОЦИТА ПЕРИФЕРНЕ КРВИ И ТКИВНА ИНФИЛТРАЦИЈА

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У раду су испитане основне имунолошке здравствено значајне промене код јединки сивог пацова из урбаних станишта (укупан број и диференцијални састав, као и активност леукоцита периферне крви, ткивна инфилтрација леукоцита и патохистолошке промене). Упоредо су рађена испитивања на неколико лабораторијских сојева пацова да би се стекао увид у ефекте спољашње средине на здравље јединки из природних популација. Промене у броју и активности леукоцита, као и инфилтрација у органе су примећене само код јединки из природних популација и указују на системску и ткивну инфламацију код тих јединки. Код већине оболелих јединки је показана повезаност ових промена и хроничних инфламаторних обољења плућа и бубрега.