of ^{59}Fe in bone falls below the control value but shows no additional reduction with increasing exposure[4]. It is assumed that this represents ^{59}Fe taken up in storage or other radioresistant sites, and these uptakes will be referred to as 'baseline' uptakes. Therefore, the net uptake will be the total uptake minus the baseline uptake. The results will be presented as two factions: the ratio of the total uptakes of irradiated to control and the same ratio of the net uptakes.

Results. Rat bones may be divided into 2 classes; those which show a reduction in ^{59}Fe uptake following exposure and those insensitive bones which show no reduction following irradiation[4]. All of the sensitive bones will be presented here. The control iron uptakes and the baseline uptakes for these samples are presented in the table in terms of percentages of the injected ^{59}Fe. A plot of the fraction of total control uptake with time post-exposures is presented in figure A. It may be noted that among the bones considered, the femur and sternum show greater reductions in uptake than the scapula or cervical spinal segments. This is similar to the results reported by Holá[2]. However, when the ratios of the net uptakes are plotted, as in figure B, these differences in response of the minima are reduced.

Also, it may be noted that the minimum in uptake for each bone occurs between 16 and 24 h post-exposure. This type of response was noted for all radiosensitive bones even with differing dose rates (8.2 R/min. and 116 R/min.). Whole-body exposures of 100 R and 300 R gave similar results. The only notable difference was a more pronounced minimum at 24 h post-irradiation, and a delayed return toward normal uptake values.

Discussion. The uptake of ^{59}Fe in the femur or tibia may be considered as being representative of the erythropoietic activity of the total skeleton in irradiated rats as long as the baseline activity has been subtracted. The minima in uptake in this study occur earlier than those reported by Holá et al. However, others have reported maximum responses at 24 h postirradiation[5,6]. This difference may be due to the mode of injection. Holá used an intraperitoneal injection route while an intravenous route was used in this study.

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Immunostimulation by a formula-defined diet[1]

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Summary. A formula-defined diet (diet 3, table 1) acted as an adjuvant in the response of the immune system to SRBC in the rat. Similar minimum and maximum antibody levels were measured in both males and females. In the males, the maximum was reached with diet 3 alone while females required the complementary action of diet 3 and LPS mR 595.

A sex-dependent enhancement of the uptake of tritiated thymidine (^{3}H-TdR) by hematopoietic tissues has been reported when rats were fed certain formula-defined diets[2]. Those results suggested that such formula-defined diets could also affect the response of the immune system in a sex-related manner.

We now report the effect of elemental diet 3[3] on the response of the rat immune system to sheep erythrocytes (SRBC). The composition of the diet has already been described elsewhere[4]. Anti-SRBC antibody levels were measured in the serum of male and virgin female Sprague-Dawley rats 6–7 weeks old, fed either the elemental diet or Purina laboratory chow. In addition, we investigated to what extent diet and sex modify the adjuvant effect of lipopolysaccharide (LPS) mR 595[5].

Randomized groups of 6 animals were fed as previously described[4]. SRBC[6] were resuspended at a 1:10 dilution in phosphate buffered saline (PBS) and injected i.p. (1 ml, approximately 10^8 cells). LPS was prepared in PBS and 40 µg injected ip simultaneously to SRBC. Anti-SRBC antibody content of serum was determined by passive hemagglutination 7 days later.

Results are presented in table 2. In controls fed laboratory chow, both males and females had comparable anti-SRBC antibody levels. Remarkably higher levels (by a factor of 23 on the average in the males and 7 in the females) were found in animals fed diet 3. By contrast, LPS was found

Table 1. Detailed composition of diet 3

	Grams per 100 g
Casein hydrolysate	12.560
Sucrose	46.839
Corn syrup solids (glucose oligosaccharides)	16.812
Long-chain triglycerides	11.982
Medium-chain triglycerides	2.997
Tapioca starch	5.234
Minerals	2.611
Free amino acids	0.384
Choline chloride	0.028
Water	0.553
Sodium citrate hydrous	0.656
Potassium chloride (from casein)	0.248

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to increase the antibody content only by a factor of 2 in the males fed laboratory chow and approximately 5 in the females. This indicates that the adjuvant effect of diet 3 on the response of the immune system to SRBC is considerably greater in the males but not the females than that obtained with LPS. While the combination of diet 3 and LPS did not significantly affect antibody levels in the males, it had an adjuvant effect (by a factor of 4) in the females. This shows that a complementary action of diet 3 and LPS is found in the females only. Notwithstanding these sex-related differences, both males and females showed similar minimum and maximum antibody levels. These findings may be interpreted in terms of a sex-related stimulation of the hematopoietic system by diet 3. In the males, a greater uptake of ^{3}H-TdR by the hematopoietic tissues has already been shown when animals were fed the elemental diet instead of laboratory chow[4,7]. In the females, on the other hand, a significantly lower uptake of ^{3}H-TdR by the spleen and the lymph nodes was obtained under the same nutritional conditions[2]. It appears then that diet 3 affects the cellular systems responsible for the immune response to a different extent in the males and the females. Such a dietary effect would also account for the sex-related differences observed in the adjuvant action of LPS. An alternative interpretation that antibody production or turnover is modified by the elemental diet is presently under investigation.

The influence of formula-defined diets on the response of the immune system is likely to have clinical importance. Such diets are already fed tumour-bearing patients to assure proper nutritional and systemic balance during cancerotherapy[8–10]. Of particular interest is our finding that diet 3 affects anti-SRBC antibody production to a similar and even greater extent than LPS. Lipopolysaccharides have been and are still investigated as promising adjuvants in the treatment of cancer[11].

Table 2. Effects of diet 3, sex and LPS mR 595 on the response of the immune system to SRBC in the rat

Anti-SRBC antibody levels determined in serum by passive hemagglutination				
Sex	Animals fed laboratory chow		Animals fed diet 3	
	SRBC[a]	SRBC-LPS[b]	SRBC	SRBC-LPS
Males	3.50 ± 0.85[c]	4.67 ± 0.61	8.00 ± 0.32	7.00 ± 0.45
	11[d]	25	256	128
	(6–20)[e]	(17–39)	(205–320)	(94–175)
Females	3.61 ± 0.51	5.83 ± 0.38	6.45 ± 0.37	8.50 ± 0.22
	12	57	87	362
	(9–17)	(44–74)	(68–113)	(311–422)

[a] SRBC: sheep erythrocytes (1 ml, 10^8 cells) injected i.p. [b] LPS: 40μg injected i.p. simultaneously to SRBC. [c] Mean number of wells (x) ± SE, 2 groups of 6 animals. [d] Titre as obtained by 2^x. [e] Titre range as obtained from SE of x.

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Persistance of maternally derived ^{3}H-estradiol in fetal and neonatal rats[1]

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Summary. Injection of ^{3}H-estradiol into pregnant rats resulted in fetal blood radioactivity 5 times higher than in maternal blood. Significant amounts of ^{3}H-estradiol were found in fetal blood 24 h later and in the offspring 5 days after birth.

Distribution of ^{3}H-estradiol in fetal and neonatal rat tissues has been studied extensively[2–5], but no report on the long term retention of this steroid in the blood appears in the literature. Fetal and neonatal rat plasma contains an estradiol binding plasma protein (EBP) which has a capacity for binding large quantities of estradiol[6]. Its functional significance is not well understood. High concentrations are found in fetal rats, with a rising titer as they approach term. EBP displays a half-life in postnatal blood of about 4 days and disappears by the 29th day. EBP is found in low concentrations in pregnant rats, but is absent in nonpregnant adults[7]. Removal of ^{3}H-estradiol from the blood of nonpregnant adults is fairly rapid[8], but because of the presence of EBP one might suspect the retention of this steroid in the blood of fetal and neonatal rats could be longer.

Döhler and Wuttke found serum estradiol was greater in 1- and 2-day-old neonates than in any other age group, including adults[9]. Estradiol values declined slowly for several days, and then rose to moderately high levels by day 10. The authors were unable to explain this pattern. The declining estradiol levels parallel a known drop in circulating EBP and may be casually related to it. The estrogen in the offspring could result from placental transfer of maternal estrogen prior to parturition. The present study reports the long term retention of ^{3}H-estradiol in the blood of fetal and neonatal rats following injection of this steroid into the mother.

Materials and methods. Sprague-Dawley rats, 20 days pregnant, received i.v. 0.5 μCi ^{3}H-estradiol/g of b.wt. The estradiol (91.3 Ci/mM, New England Nuclear) was checked for purity by TLC prior to use. Injected animals were decapitated and their fetuses removed and kept cold until blood samples could be taken. Adult and fetal blood

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