though attempts to isolate an L1210-associated virus have been unsuccessful[19].

In conclusion, the PFC kinetic pattern in leukemic mice indicates that growth of L1210 leukemia does not depress the primary humoral antibody response of the host, unless the antigenic stimulus is given at a later stage of tumor development. In such case moderate immunosuppression was observed at 4 days after administration of the antigen.

Riassunto. La risposta immunitaria primaria a globuli rossi di montone, studiata mediante la tecnica delle placche di Jerne in topi CDF_1 normali o portatori di leucemia L1210, indica che lo sviluppo neoplastico deprime la formazione di anticorpi umorali solo nel caso in cui l'antigene venga iniettato in fase avanzata della malattia.

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Androgens and Erythropoiesis in Bone Marrow. II. Effect of Testosterone Propionate on ^{59}Fe Concentration in Erythrocytes and Bone Marrow

The erythroid maturation of bone marrow in young, adult, Lewis male rats revealed a shift from polychromatic and orthochromatic normoblasts to basophilic normoblasts beginning 4 weeks after gonadectomy. Such a distribution of normoblasts returned to normal after the rats were injected s.c. with testosterone propionate daily for 7 days[1].

The transit time (maturation time) of polychromatic and orthochromatic normoblasts in bone marrow of normal rats was estimated to be 22 h while the transit time of pronormoblasts, basophilic normoblasts, polychromatic and orthochromatic normoblasts accounted for a total of 73 h[2]. The rate of division of erythroid stem cells and/or their precursors, leading to differentiation of pronormoblasts, was accelerated by erythropoietin (ESF) in 5-FU treated mice and the first ESF-dependent erythrocytes appeared in the peripheral blood 3 days following ESF administration[3]. Erythropoietin production increases following testosterone administration and this is considered, at least in part, the determining factor for the erythropoietic activity of androgens[4].

In view of these premises we investigated the time of the earliest erythropoietic effect induced by administration of testosterone propionate to young, adult Lewis male rats gonadectomized 4 weeks before. The hormone was injected s.c. at the dose levels and regimens indicated in tables. The total volume of each injection was 0.5 ml based on SSV (mixture of isotonic saline, polysorbate 80, carboxymethylcellulose and benzyl alcohol). The erythropoietic activity was expressed as percent of ^{59}Fe uptake by erythrocyte and bone marrow following intracardial administration of 1 μc of ^{59}Fe in 0.5 ml saline. The ^{59}Fe was administered with the hormone, when it was given in a single administration, and with the last injection of testosterone propionate, when the animals were treated daily for 7 days.

The animals were sacrificed by etherization immediately after the blood was taken and the bone marrow was blown out, with a 5 ml syringe, from the right femur with a No. 18 gauge needle. The marrow was then weighed and treated for measurement of radioisotope[5]; radioactivity was counted in a well-type liquid scintillator counter. An 0.1 ml aliquot of red cells washed 3 times with saline was used for measuring ^{59}Fe uptake by the same method employed for the bone marrow determination. The ^{59}Fe uptake has been reported as percent of total dose injected into whole circulating erythrocyte (2.37 ml erythrocyte/100 g body wt.) and per 100 mg of bone marrow.

Each experiment was duplicated. The results were reported as means $\pm$ S.D. and the Student's test was used for determining p value. Any change showing $p < 0.01$ was considered significant.

Measuring ^{59}Fe uptake 24 h following the radioiron administration (Table I) revealed an enhancement of erythropoietic activity due to 0.4 mg of testosterone propionate injected daily for 7 consecutive days. The ^{59}Fe content decreased in bone marrow and increased in erythrocytes. When radioactivity was measured at 48 and 72 h after ^{59}Fe administration any changes that might have occurred were apparently overcome by the on-going normal rate of erythroid maturation. The 24 h change of ^{59}Fe content in erythrocytes and bone marrow characterized the erythropoietic effect of testosterone propionate in animals with erythropoiesis impaired only by large depletion of endogenous androgens (and not by any other artifact such as polycythemia or starvation). The results could be revealing the cumulative effect of repeated doses of testosterone propionate rather than an immediate effect of the steroid.

The injection of different amounts of testosterone propionate given in single doses to gonadectomized animals showed that a s.c. injection of 1.6 mg of the androgen simultaneously with 1 μc of ^{59}Fe injected intracardially still depletes radioiron from bone marrow and increases its content in erythrocytes within 24 h (Table II). In additional trials bleedings prior to 24 h were tested but no significant changes of ^{59}Fe incorporation were noticed.

These findings are in agreement with the morphological changes previously observed in bone marrow[1]. In fact, since the transit time of polychromatic and ortho-

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Table I. Effect of different bleeding schedules on ^{59}Fe uptake following testosterone propionate administration

Group	No. of rats	Hours after ^{59}Fe injection	^{59}Fe uptake, % of injected dose	
			In erythrocytes	In 100 mg of bone marrow
Vehicle control	8	24	20.4 ± 6.1	1.51 ± 0.11
Testosterone propionate	8		37.1 ± 9.4[a]	1.07 ± 0.27[a]
Vehicle control	8	48	59.1 ± 8.8	0.40 ± 0.11
Testosterone proprionate	8		66.0 ± 9.1	0.19 ± 0.05[a]
Vehicle control	8	72	55.5 ± 6.2	0.19 ± 0.05
Testosterone propionate	8		63.3 ± 10.7	0.19 ± 0.04

An 0.4 mg daily dose of hormone was injected s.c. for 7 consecutive days in male Lewis rat, 85–90 days old and gonadectomized 4 weeks prior to treatment. 1 μc of ^{59}Fe in 0.5 ml saline was injected simultaneously with the last treatment. [a] $p < 0.01$ when compared with the correspondent vehicle control group.

Table II. Effect of a single s.c. injection of testosterone propionate (TP) on erythropoiesis of male Lewis rats, 85–90 days old and gonadectomized 4 weeks prior to treatment

Group	Treatment Compound	Dose (mg)	No. of rats	^{59}Fe uptake, % of injected dose	
				In erythrocytes	In 100 mg of bone marrow
Intact	Vehicle	0.5 ml	8	41.0 ± 11.7	1.38 ± 0.38
Castrated	Vehicle	0.5 ml	8	41.1 ± 6.8	1.24 ± 0.42
Castrated	TP	0.2	8	44.1 ± 8.9	1.07 ± 0.22
Castrated	TP	0.4	8	39.8 ± 5.7	0.78 ± 0.40
Castrated	TP	0.8	8	43.1 ± 10.7	0.95 ± 0.27
Castrated	TP	1.6	8	53.0 ± 9.0[a]	0.65 ± 0.11[a]

1 μc of ^{59}Fe in 0.5 ml saline was injected intracardially and simultaneously with testosterone propionate. The animals were bled and sacrificed 24 h later. [a] $p < 0.01$ when compared with castrated vehicle control group.

chromatic normoblasts is 22 h we must assume that the increased ^{59}Fe content of circulating erythrocytes in the present studies represented an accelerated maturation of late basophilic normoblasts or early polychromatic normoblasts. These results appear to be independent of any direct effect of testosterone propionate on the release or activation of ESF. Erythropoietin, in fact, would have enhanced ^{59}Fe uptake in new erythrocytes 3 days following hormone administration. However, the increased release of ESF following androgen administration[4] must be initiated through the feedback mechanism existing between erythrocyte and stem cell system[6]. In other words, the reduced proportion of polychromatic and orthochromatic normoblasts in bone marrow following testosterone propionate would require the presence of additional ESF for the differentiation of new erythroid elements, substituting for the depleted ones.

Résumé. L'augmentation d'incorporation de ^{59}Fe dans les globules rouge de rats auxquels on a donné du testosterone propionate est évidente dans la circulation périphérique du sang, 24 h après l'injection du ^{59}Fe. Le rapport entre cette donnée et le temps de transfert des erythroblastes dans la moelle osseuse montre que les androgènes stimulent la maturation de normoblastes basophiliques et polychromatophiliques, plutôt que l'érythropoietine.

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Suppression of Antibody Formation Against Sendai Virus in the SV_{40} and Adenovirus 16 Infected Hamsters

The immunosuppressive effect of mouse leucosis viruses was recently observed both in respect to antibody formation and immune responses of the delayed type[1–3]. The same effect was discovered for measles and rubella viruses[4, 5]. The results of the experiments presented below show marked suppression of antibody formation against Sendai virus caused by SV_{40} and adenovirus type 16.

Materials and methods. We used 2-month-old male Syrian hamsters of our own laboratory breeding. Papovavirus SV_{40}, strain A 426, was received from the Museum of Oncogenic Viruses of the Institute of Experimental and Clinical Oncology AMS, USSR in 1963 and maintained in our laboratory in green monkey kidney cell cultures. The titre of the virus was 5×10^7 $TCPD_{50}$/0.1 ml.