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.

Human adenovirus type 16 (strain 663) was kindly provided by Dr. R. S. Dreizin. The virus was passaged in Hela cell cultures. Its titre was determined by the cytopathogenic effect which occurred at 8–12 days after the infection of the monolayer. It amounted to 10^3 $TCPD_{50}$/0.1 ml.

Parainfluenza virus Sendai (5×10^8 D_{50}) was multiplied in allantoic cavity of 9-day embryonated eggs. The haemagglutinating activity of Sendai virus was 5120 haemagglutinating units (HU) per 1 ml.

The haemagglutination inhibition (HI) reaction was performed using 0.25 ml of serum dilution, 0.25 ml of virus suspension containing 2 HA units and 0.5 ml of 1% suspension of chick erythrocytes. Isotonic saline was used as diluent. The test was carried out at 4 °C and at room temperature. The HI titre was expressed as reciprocal of the highest initial dilution of serum showing inhibition of haemagglutination, i.e., it was related to a volume of 0.25 ml.

Results and discussion. The hamsters were inoculated i.p. either with SV_{40} or with human adenovirus type 16. The corresponding groups of control hamsters remained uninoculated; 9 days later the hamsters of inoculated and control groups (each group having 8–10 animals) were immunized i.p. with 0.5 ml of active Sendai virus. At different times after the Sendai virus inoculation, the sera of hamsters were checked for anti-Sendai antibodies by means of HI test.

The data presented in Figure 1 show that at 15 and 23 days after the Sendai virus immunization the mean geometrical titres of antihaemagglutinins expressed in logarithm with base 10 were considerably lower in the sera of animals previously inoculated with SV_{40} or adenovirus type 16 as compared with those in the sera of control animals which had been immunized with Sendai virus alone. The results obtained were statistically significant.

Figure 2 shows the results of the second experiment when the following groups of animals were used: 1. animals immunized with Sendai virus after previous inoculation with SV_{40}, 2. animals immunized with Sendai virus after previous inoculation with culture fluid of non-infected green monkey kidney, 3. animals immunized with Sendai virus alone, 4. animals immunized simultaneously i.p. with SV_{40} and Sendai virus.

As seen from Figure 2 the sera of the animals first inoculated with SV_{40}, and 9 days later with Sendai virus, revealed mean geometrical titres of antihaemagglutinins considerably lower than those of the control animals immunized with Sendai virus alone. Figure 2 shows that simultaneous i.p. inoculation with SV_{40} and Sendai virus as well as previous inoculation with culture fluid of non-infected green monkey kidney failed to affect the level of the specific antibodies. It is of interest to note that i.p. inoculation of SV_{40} to adult hamsters failed to influence in any way the total amount of leucocytes in peripheral blood.

Suppression of antibody formation against Sendai virus in hamsters previously inoculated with SV_{40} or adenovirus 16 is due to the immunosuppressive activity of the above viruses. However, when, as in this case, an active virus serves as a test antigen, the whole situation may be associated with some more complicated mechanisms.

The absence of the effect in the experiments when SV_{40} and Sendai viruses were injected simultaneously, and its marked manifestation in those when Sendai virus was injected after SV_{40} inoculation, suggest an immunosuppressive character of the phenomenon. The remarkable fact is that the suppression occurred on the 9th day after the injection of SV_{40} or adenovirus type 16. It is in that time that hamsters acquired a strong resistance against the transplantation of the corresponding virus-induced tumours.

The immunosuppressive effect revealed by 2 DNA-containing viruses of different oncogenic activity seems to support a suggestion[6–8] that the inhibition of the immunological response is a condition indispensible for both carcinogenesis and malignant growth. As we showed

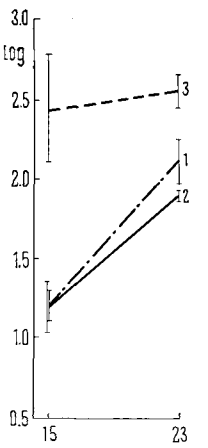

Fig. 1. Effect of previous SV_{40} and adeno 16 infection of hamsters on the antihaemagglutinins mean titre of Sendai virus at 15 and 23 days after immunization (mean geometrical titres expressed in logarithms with base 10). 1. In animals inoculated with SV_{40}; 2. in animals inoculated with adenovirus 16; 3. in control animals immunized with parainfluenza virus Sendai alone.

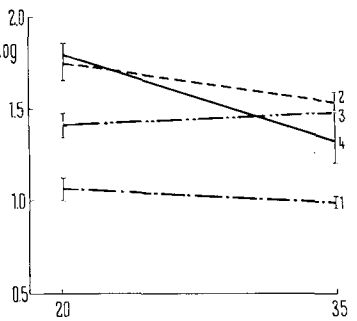

Fig. 2. Effect of previous inoculation of hamsters with SV_{40} on the antihaemagglutinins mean titres of Sendai virus at 20 and 35 days after immunization. 1. In animals previously inoculated with SV_{40}; 2. in animals previously inoculated with culture fluid of non-infected green monkey kidney cell culture; 3. in animals immunized with Sendai virus alone; 4. in animals inoculated simultaneously with SV_{40} and Sendai virus.

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elsewhere, the intracardiac inoculation of animals with SV_{40} stimulated the growth of transplantable carcinogen-induced tumours[9]. This observation, as well as the capacity of the above virus to intensify the carcinogenicity of DMBA in new-born hamsters[10], may have something to do with the immuno-suppressive property of SV_{40}.

An immunosuppressive effect of DNA-containing viruses seems to account for the fact that tumours induced by them grow inspite of the existence of strong transplantation antigens on their surface.

A preliminary experiment in which sheep erythrocytes were injected to hamsters 9 days before inoculated with SV_{40} has shown a marked suppression of antibody formation against the above erythrocytes.

Выводы. Золотистых хомячков заражали вирусами SV_{40} или адено типа 16. Через 9 дней после заражения им вводили живой парагриппозный вирус Сендай. У этих животных наблюдалось подавление антителообразования к вирусу Сендай по сравнению с контрольными.

В связи с полученными данными кратко обсуждается проблема иммунодепрессивного действия онкогенных вирусов.

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Phagocytosis of ^{14}C Dinitrophenyl Poly L-Lysine by Peritoneal Exudate Cells from Guinea-Pigs

Guinea-pigs of strain II and strain XIII respond differently to synthetic antigens, as demonstrated by the experiments of LEVINE and BENACERRAF[1], and BEN-EFFRAIM, FUCHS and SELA[2]. Hapten conjugates of poly L-lysine, for example, elicit an immune response in strain II, but fail to do so in strain XIII; this facility being a dominant autosomal unigenic trait. It is pertinent to the question of whether or not phagocytosis is involved in antibody synthesis[3–5] to determine if these strains also differ in their ability to process poly L-lysine conjugates this way. A direct correspondence between phagocytic ability and antibody synthesis would obviously accord with the participation of both phagocytic and lymphocytic cells in the immune response. Were no difference to be found in the phagocytosis of the antigen by responsive and non-responsive strains, one must infer, either that the state of unresponsiveness is attributable to a post-phagocytic block in antibody synthesis, or else phagocytosis has no relevance to the immune response.

Data are presented that demonstrate the ability of peritoneal exudate cells from strain II and XIII guinea-pigs to phagocytize ^{14}C dinitrophenyl poly L-lysine (^{14}C-DNP-PLL). The DNP-PLL used was prepared as described by LEVINE and BENACERRAF[6]. PLL was kindly given by Prof. P. DOTY, Harvard University, and had an average degree of polymerization of 398. Uniformly labelled ^{14}C-DNP (Amersham; 34 μc/mg) was employed as the hapten. On the average, twelve ^{14}C-DNP groups were substituted per molecule of PLL to form ^{14}C-DNP_{12}-PLL_{398}.

Male guinea-pigs (approx. 800 g) were injected i.p. with 20 ml 1% sodium chloride and 0.1% glycogen, 3 days before being sacrificed. 4 h prior to sacrifice, 2.6 mg ^{14}C-$DNP_{12}PLL_{398}$ was administered i.p. The peritoneal contents were washed with 170 ml chilled Hanks solution, which was subsequently filtered through several layers of cheese cloth. The cells were harvested by centrifugation at 700 rpm for 20 min in a swinging-bucket International centrifuge at 5 °C. The pellet of cells obtained was resuspended with 0.5 ml Hanks solution. A differential cell count of the peritoneal exudate from animals of both strains, revealed that polymorphonuclear cells, monocytes and lymphocytes were present in about equal proportions. Samples were taken from the cell suspensions and then spotted and dried on Whatmann No. 540 filter discs. The radioactivity present was determined in an Ansitron liquid scintillation spectrophotometer.

The results of the experiment are given in the Table. It can be seen from these data that the strains manifested no apparent difference in their ability to phagocytize ^{14}C-$DNP_{12}PLL_{398}$. That the radioactivity observed in these cell preparations represents phagocytosis and not simply adherence of antigen to cell surfaces is indicated by the fact that further washings of the cells did not diminish their radioactivity. The yield of cells from these guinea-pigs was low when compared with the yields obtained from rats 72 h following beef heart infusion broth i.p. and, in addition, the relative proportion of monocytic cells was less[7]. However, the efficiency of phagocytosis was observed to be about 1–2% of antigen administered and this

Extent of phagocytosis of ^{14}C $DNP_{12}PLL_{398}$ by peritoneal exudate cells from strain II and XIII guinea-pigs

Strain	Peritoneal No. cells	Exudate cpm	Uptake ^{14}C DNP-PLL (μg per 10^7 cells)
II	0.28×10^7	15,420	33.9
XIII	0.30×10^7	16,900	35.1

4 h prior to sacrifice, 2.6 mg ^{14}C $DNP_{12}PLL_{398}$ (1.63×10^6 cpm/mg) were injected i.p. into male guinea-pigs of strain II and XIII, 2 from each strain, that had been previously primed, 3 days before experimentation, by treatment with a saline-glycogen solution injected i.p.

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