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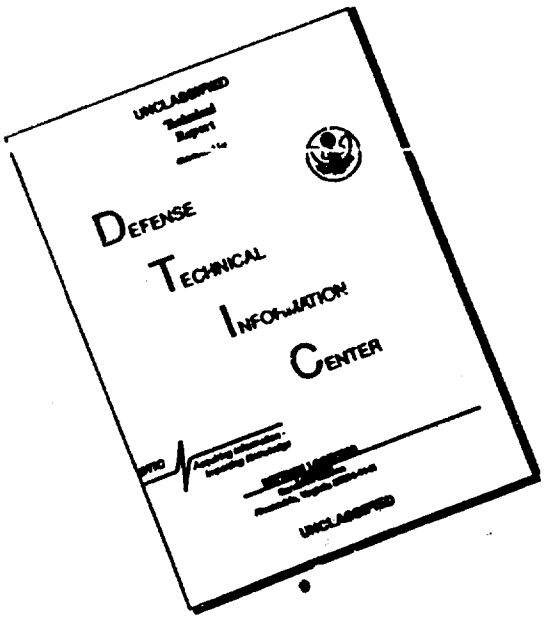

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TRANSLATION

The enteroviruses which occur in man are subdivided into three main groups: -- the poliovirus, the Coxsackie viruses and the ECHO viruses. The poliovirus group includes three immunological types. At present the Coxsackie virus group includes 24 types, and the ECHO virus group lists 28 types.

The distinctive property of the poliovirus strains is that in monkeys they can produce paralysis with characteristic histological picture. The ECHO virus group's strains which cause cytopathogenetic effect in tissue cultures were put in a separate group because of their pathogenicity for laboratory animals. For a long time it had been thought that one of the basic properties of the Coxsackie virus group was their ability to cause myositis in newborn white mice, while they remained harmless for monkeys.

The first information on the non-homogenous character of the Coxsackie virus group was gained by M. P. CHUMAKOV and coworkers (1) when, -- in their experiments on monkeys, adult cotton rats (Sigmodon hispidus), and suckling white mice -- they isolated strains of a Type IV poliovirus from poliomyelitic patients; according to the data of JOHNSSON and LUNDMARK (2), this type was immunologically similar to the Coxsackie A-7 virus. In the laboratories of HABEL, HORSTMANN, K. IONESCU-MIHAEST (personal communication), studies of the AB-IV strain cooroborated its marked pathogenicity for monkeys (3; 4). Now, in the USA (5) and in England (6), the role of the Coxsackie A-7 virus in the etiology of poliomyelitis is definitely established.

Other strains of the Coxsackie A-7 virus were also pathogenic for monkeys. Among them is the prototype of the WP strains isolated by DALLDORF in 1948 (7; 8).

(Page 48) The non-homogeneity of the ECHO virus group is shown, for instance, in the ECHO-9 and ECHO-10 virus types. A number of strains of ECHO virus Type 9 cause myositis in suckling white mice. From other representatives of the ECHO group ECHO-10 differs by its particle size and by its pathogenicity for sucking white mice; at the present time, it is transferred to the group of reoviruses.

The non-homogeneity of the enterovirus groups prompted us to study in 1957 the pathogenicity of the Coxsackie virus group for laboratory animals, and in 1958 that of the ECHO virus group. The comparative antigenic activity of these viruses was also studied in rabbits and type-specific immune sera were obtained.

Title: Study of the ECHO and Coxsackie group of enteroviruses in laboratory animals.

Author: V.I. Zhevandrova et al.

Source: Akademia nauk latviiskoi SSR (Institue of Microbiology) p. 47-59 Riga, 1962

TABLE 1

PROTOTYPIC STRAINS OF THE ECHO AND COXSACKIE VIRUSES

ECHO viruses

Type	Prototypic strain	Author
1	Faruk	Melnick
2	Cornelis	Melnick
3	Morrisey	Melnick
4	Pezachek	Melnick
5	Nois	Melnick
6	d'Amori	Melnick
7	Wallace	Ramos-Alvarez
8	Brisson	Sabin
9	Hill	Sabin
10	Lang	Sabin
11	Gregori	Sabin
12	Travis	Hammon, Ludwig
13	Hemphill	Hammon, Ludwig
14	Gay	Melnik
15	CH-9651	Ormsby, Melnick
16*		
17	CHEE-29	Ramos-Alvarez, Sabin
18	Metcalf	Ramos-Alvarez, Sabin
19	Bark	Ramos-Alverez, Sabin

COXSACKIE viruses

GROUP A:

1	FS 48249	Dalldorf
2	FL 49190	Dalldorf
3	J.01.49191	Dalldorf
4	50246	Hount & Benefield
5	GS 5134	Dalldorf
6	CG 5134	Dalldorf
7	WP 50140	Dalldorf
8	CD 5010	Dalldorf
9	PB 50546	Dalldorf
10	nk 50548	Dalldorf
11	1 - 52148	Goden & Kurnen
12	12-51204	Contreras
	Texas	Barnet & Melnick
13	Flores 5359	Dalldorf
14	G-14 52113	Gir & Misrokh
15	G-9 52108	Gir & Misrokh
16	G10- 52109	Gir & Misrokh
17	G-12 52111	Gir & Misrokh
18	G-13 52112	Gir & Misrokh
19	P-N 53153	Hubner

GROUP B:

1	PO 49683	Dalldorf
2	Ogaio 50207	Melnick et al.
3	Nancy 50531	Melnick et al.
4	JVB 51196	Dalldorf
5	Folkner 53122	Steigmann

(Page 49) MATERIAL AND METHODS . - The Prototypic and domestic strains of 18 types of ECHO viruses, and 24 types of Coxsackie viruses were studied (Table 1 and 2).

TABLE 2.

STRAINS OF ECHO AND COXSACKIE VIRUSES ISOLATED IN THE USSR AND STUDIED IN RESEARCH ANIMALS

Virus type	Name of strain	Diagnosis of disease in which the strain was found	Place of origin	Author
ECHO-4	Muzlanov	Poliomyelitis	Moscow	M.K.Voroshilova
ECHO-6	Strel'nikova	Healthy child	Saratov	M.K.Voroshilova
ECHO-9	Kapustin	Healthy child	Saratov	M.K.Voroshilova
ECHO-9	Pokrovskii	Poliomyelitis	Moscow	M.K.Voroshilova
ECHO untyped	D'yakova	Poliomyelitis	Karaganda	E.A.Tol'skaya
AB-IV Coxsackie A-7	ZhG	Poliomyelitis	Karaganda	E.A. Tol'skaya
AB-IV Coxsackie A-7	NP	Poliomyelitis	Karaganda	E.A.Tol'skaya
AB-IV Coxsackie A-7	OKh	Poliomyelitis	Karaganda	E.A.Tol'skaya
Coxsackie A-9	Nesterov	Febrile disease	Moscow	M.K.Voroshilova
Coxsackie A-9	Starova	Paralytic disease	Moscow	A.P.Belyaeva
Coxsackie B-3	Palii	Poliomyelitis	Moscow	A.P.Belyaeva
Coxsackie B-4	Maevskaya	Healthy child	Sukhumi	M.K.Voroshilova
Coxsackie B-4	Manchenko	Healthy woman	Sukhumi	M.K.Voroshilova
Coxsackie B-5	Borisova	Poliomyelitis	Moscow	M.K.Voroshilova

Domestic strains of ECHO viruses were isolated in 1955 by M.K.VOROSHILOVA, meanwhile the Type 6 (Strel'nikova) and Type 9 (Kapustin) ECHO viruses were isolated from healthy children. The Pokrovskii strain of the ECHO-9 virus was isolated from the feces of a polio patient. The ECHO-4 strain was obtained from the Muzlanov strain which was isolated from a patient with paralytic poliomyelitis. For a long time this strain could not be typed by neutralization tests on tissue cultures. At its study in animals, it was pathogenic for newborn and adult white mice. Histological studies showed changes characteristic for experimental poliomyelitis in white mice. After mouse passages, it was typed as a Type II poliomyelitis virus. The Muzlanov strain was then subdivided according to the plaque method. Its second constituent was the ECHO-4 virus which was studied in research animals.

(Page 50) The Coxsackie A-9 (Nesterova) virus strain was isolated in 1955 from a patient with febrile disease, and the Coxsackie B-4 (Maevskaya & Manchenko) strain was isolated in 1957 from healthy virus carriers.

The Coxsackie B-5 (Borisova) strain was isolated from the feces of a poliomyelitic patient who had a slight spinal form of the disease, with changes in the electromyogram (10). The immunological identity of the studied strains was confirmed by neutralization tests, by using standard immune sera obtained from the World Health Organization.

Ten percent suspensions of the cadavers of suckling white mice killed at the peak of the disease (Coxsackie viruses), culture fluids from cultures of trypsinized monkey kidneys (ECHO viruses), or virus-containing suspensions of focalia (the GZh, PN, KhO strains) served as viral material. The trypsinized monkey-kidney cultures were prepared according to generally accepted methods. The virus in cultures was concentrated in the No. 199 medium which was kept at pH= 7.8, and was prepared with Earle's solution.

The time of occurrence of the sytcpathogenic effect in trypsinized kidney culture, the incubation period in suckling white mice as well as the virus titres are shown in Table 3.

TABLE 3.

CYTOPATHOGENIC EFFECT AND TITRES OF THE ECHO AND COXSACKIE VIRUS GROUPS

	Тип вируса ECHO	Титр вируса в 1г TCD_{50}	Сроки наступления цитопатогенного действия в часах	Тип вируса Коксаки А	Титр вируса у сосунков белых мышей в 1г LD_{50}	Инкубационный период у сосунков белых мышей в часах	Тип вируса Коксаки В	Титр вируса: у сосунков белых мышей в 1г LD_{50}	Титр вируса: в культуре трипсинизир. почки обезьяны в 1г TCD_{50}	Инкубационный период у сосунков белых мышей в часах	Сроки наступления цитопатог. действия в часах
	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)	(k)
1	7.3	48	1	7.4	48	B-1	6,0	6.3		72	72
2	7.3	48	2	8.0	48	2	6.2	6.2		48	72—96
3	6.3	48—72	3	8.0	48	3	—	5.8		48	72
4	4.8	72—96*	4	8.0	48	4	6.6	6.5		48	72—96
5	7.3	48	5	7.7	48	5	5,7	5.3		72—96	72
6	7.3	48—72	6	7,0	48						
7	6.8	48—72	7	5.4	72						
8	7.3	48—72	8	8,0	48—72						
9	6.8	48—72	9**	—	48—72						
10	5.3	72*	10	8,0	48						
11	7.3	48	11	7.0	72—96						
12	6.3	48	12	7.8	48						
13	6.8	48	13	6.2	48—96						
14	5.3	48—72*	14	6.6	48—72						
15	5.8	72	15	5.9	72						
17	5.3	72*	16	7.0	48						
18	4.8	72*	17	7.2	48						
19	7.3	72	18	7.0	72						
			19	7.1	48—72						

HEADINGS:
- a. Type of ECHO virus
- b. Virus titre in 1 gram TCD_{50}
- c. Time of occurrence of cytopathogenic effect in hours
- d. Type of Coxsackie A virus
- e. Virus titre, in suckling white mice, in 1 gram TCD_{50}
- f. Incubation period in suckling white mice in hours
- g. Type of Coxsackie B virus
- h. Virus titre in suckling white mice in 1 gram LD
- i. Virus titre in trypsinized monkey kidney culture, in 1 gram TCD_{50}
- j. Incubation period in suckling white mice in hours
- k. Time of occurrence of cytopathogenic effect in hours

* Viruses which do not cause full degeneration of cells in the indicated time.

** The titre of the Coxsackie A-9 virus in trypsinized monkey kidney culture was equal to 7.3 TCD_{50}; the time of appearance of the cytopathogenic effect was 48 hours.

The prototypic and domestic strains of the Coxsackie and ECHO viruses were studied in experiments on adult and newborn white mice, cotton rats, guinea pigs, and rabbits. The domestic strains were also studied on monkeys by way of experimental combined infection of brain, spinal cord, tonsils, and muscles.

The pathogenicity for small laboratory animals was studied by way of initial infections of the animals and in single silent passages. Both at the initial viral inoculation and in the silent passage, each animal was

infected in brain and muscle. In suckling white mice the virus was subcutaneously introduced. The silent passages were made with emulsions separately prepared from the brain, the muscles, and the organs of a few animals killed on the seventh day after infection. The animals were kept under observation for 2 to 4 weeks. The brain, the spinal cord, the muscles and the internal organs were submitted to histological examination.

For the determination of the viral antigenic activity, supplementary immunizations were made on those rabbits which were left over after the experiments for pathogenicity study. At this occasion the virus was introduced into the vein and the muscles, together with an additive (9 parts of "Baiol F", one part of "Arlatsel A", 10 parts of antigen). At the immunization with ECHO viruses, seven injections were made; at the immunization with Coxsackie viruses, eleven injections were made (Table 4). Moreover, it was determined that the antigenic activity of the ECHO-7 and ECHO-9 viruses somehow depends upon the mode of their introduction into the rabbits.

The virus was six times inoculated at seven day intervals, each time 10 ml, into the vein, the muslces, the heart, or with the additive into the vein and the muscles. The sera of two-three rabbits were pooled. The titres of the obtained immune sera were determined by neutralization tests on suckling white mice, or by the cytopathogenic effect in tissue cultures. The titre of a serum was considered its highest dilution whose introduction protected the suckling white mice from death, or prevented the appearance of the cytopathogenic effect by 100 TCD_{50} of the homologous virus.

RESULTS: By their pathogenicity in laboratory animals, the studied ECHO viruses form a homogenous group.

In our experiments, not a single one of the ECHO virus strains of the first 19 types [1] caused disease in cotton rats, white mice, their sucklings, guinea-pigs and rabbits.

The Type 6 and 7 ECHO viruses, introduced into these animals, were detected in considerably large titres (lg TCD_{50} = 3.0 - 4.0) in the emulsions prepared from the brain, the muscles, and the organs merely one-two hours after the infection. Further on, in one to three days, the virus titres dropped markedly, and by the seventh to tenth day the virus could not be detected in the brain, the muscles and the organs of the infected animals.

The domestic strains of the Type 4 (Muzlanov), Type 6 (Strel'nikova) and Type 9 (Kapustin and Pokrovskii) ECHO viruses as well as the Coxsackie A-9 (Nesterova, Starova), B-3 (Palii), B-4 (Maevskaya & Manchenko), and B-5 (Borisova) virus strains did not provoke paralysis in monkeys.

The Coxsackie A-1 to A-19 viruses which are pathogenic for suckling white mice were highly pathogenic for suckling cotton rats. The sensitiveness of the suckling white mice and suckling cotton rats to the Coxsackie A-14 virus was practically identical. [2]

1/ ECHO virus 16 was not studied because of its low titre.
2/ The titres of the Coxsackie A-14 virus strains No. 60/59 and No. 54/59 were equal, to wit, 6.6 and 7.7 lg TCD_{50} for suckling white mice, and 6.59 and 7.5 lg TCD_{50} for suckling cotton rats.

TABLE 4: OUTLINE OF THE IMMUNIZATION OF RABBITS

ECHO viruses

(1) Дни иммунизации	(2) Количество (в мл) и место введения вируса			
	вена (3)	мышцы (с дополнителем) (4)	мышцы (5)	итого (6)
1	1,0	10,0	—	11,0
7	1,0	—	—	1,0
14	1,0	—	—	1,0
21	1,0	5,0	—	6,0
31	1,0	—	—	1,0
52—55	1,0	10,0	—	11,0
82—85	1,0	—	2,0	3,0
				34,0

COXSACKIE viruses

Вирусы Коксаки

(1) Дни иммунизации	(2) Количество (в мл) и место введения вируса						
	A-1 — A-4				A-5 — A-8, A-10, A-12, A-14, A-15		
	вена (3)	мышцы (с дополнителем) (4)	мышцы (5)	итого (6)	вена (3)	мышцы (с дополнителем) (4)	итого (6)
1	1,0	10,0	—	11,0	1,0	10,0	11,0
2	2,0	—	2,0	3,0	1,0	—	1,0
3	1,0	—	2,0	3,0	1,0	—	1,0
7	1,0	—	2,0	3,0	1,0	—	1,0
8	1,0	—	2,0	3,0	1,0	—	1,0
9	1,0	—	2,0	3,0	1,0	—	1,0
17	1,0	5,0	—	6,0	1,0	5,0	6,0
18	1,0	—	2,0	3,0	1,0	—	1,0
19	1,0	—	2,0	3,0	1,0	—	1,0
35	1,0	5,0	—	6,0	1,0	5,0	6,0
42	1,0	—	—	1,0	1,0	—	1,0
				45,0			31,0

LEGEND OF HEADINGS: 1. Day of immunization; 2. Amount (in ml) and site of the virus inoculation; 3. Vein; 4. Muscles (with additive); 5. Muscles; 6. TOTAL.

At histological examination of eight suckling white mice and twelve suckling cotton rats, infected with Coxsackie A-14 strains, no changes were found in the central nervous system. In all cases only such manifestations of myositis were noticed which are characteristic for all the viruses of the Coxsackie A-group.

Less sensitive are the suckling cotton rats to viruses of the Coxsackie B group. These viruses do not regularly cause sickness in suckling cotton rats, and can be easily adapted to these animals in a silent passage.

Just as the ECHO viruses, none of the studied Coxsackie A and B virus strains (except Coxsackie A-9), caused any clinically marked disease in white mice, guinea pigs, rabbits, and cotton rats (Table 5).

Just as the prototypic strain of the Coxsackie A-14 , the AB-IV - Coxsackie A-7 group of virus strains (OKh, ZhG, NP) have marked pathogenicity for adult cotton rats whose lower extremities become paralyzed, and in their brain and spinal cord histological changes occur which are characteristic for experimental poliomyelitis (Figure 1).

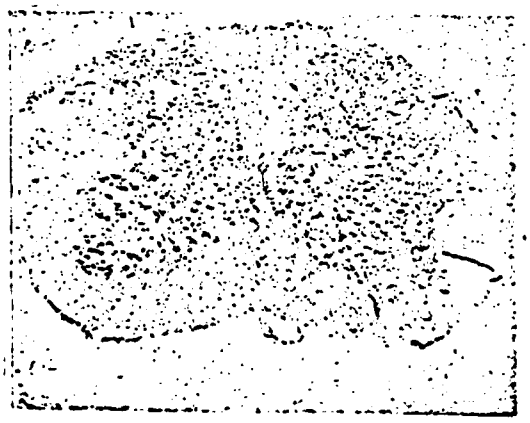


FIGURE 1: Diffuse inflammatory reaction, outfall of motor neurons, dystrophic changes of neural cells in the anterior horn of the spinal cord of a cotton rat infected with Coxsackie A-14 virus. Magnification 10 x. Staining by Nissl's method with cresyl violet.

By their pathogenicity for adult cotton rats the AB-IV-Coxsackie A-7 and A-14 virus strains markedly differ from other viruses of the Coxsackie group. In these animals, with complete absence of a lesion in the muscles, neurotropic properties of the mentioned strains are clearly manifested.

The Coxsackie A-7 and A-14 virus strains also stand by themselves in regard to their pathogenicity for monkeys.

Each of the studied viral strains in the AB-IV-Coxsackie A-7 group causes paralytic affection in monkeys. At histological examination of the monkeys infected with the ZhG and NP strains, the central nervous system, especially the spinal cord, showed diffuse inflammatory degenerative changes whose character was similar to the changes encountered in poliomyelitis. Lesions were detected in the frontal, temporal, parietal areas of the cortex, in subcortical formations, in mesencephalic nuclei, in the pons, the oblongata, and the cerebellum.

TABLE 5:

PATHOGENICITY OF THE COXSACKIE A AND B VIRUSES FOR LABORATORY ANIMALS

Таблица 5

Патогенность вирусов Коксаки А и В для лабораторных животных

1 Штаммы вирусов Коксаки	2 Первичное заражение: 3 хлопковые крысы	4 белые мыши	5 сосунки хлопковых крыс	6 Немой пассаж: 7 хлопковые крысы: 8 головной мозг: опыт 11	8 головной мозг: контроль 12	9 тушка: опыт 11	9 тушка: контроль 12	8 белые мыши: головной мозг: опыт 11	8 головной мозг: контроль 12	9 тушка: опыт 11	9 тушка: контроль 12
				Группа А GROUP							
1	0/9	0/6	+	0/6	—	0/6	—	0/8	+	0/10	+
2	0/8	0/7	+	0/10	—	0/6	—	0/10	—	0/8	—
3	0/6	0/7	+	0/6	—	0/6	+	0/7	0	0/8	—
4	0/10	0/6	+	0/6	+	0/6	+	0/8	+	0/8	—
5	0/10	0/10	+	0/6	+	0/6	+	0,8	+	0/7	+
6	0/18	0/10	+	0/6	—	0/6	+	0/8	—	0/5	—
7	+	0/9	+	+	+	+	+	0/8	—	0/8	—
8	0/10	0/8	+	0/6	+	0/6	+	0/7	—	0/8	—
9	0/10	+	+	0/6	0	0,6	0	0/20	+	0/20	+
10	0/6	0/7	+	0/5	—	0/5	—	0/8	—	0/7	—
11	0/3	0/7	+	0/6	—	0/6	—	0/8	—	0/7	—
12	0/9	0/7	+	0/6	—	0/5	—	0/8	+	0/9	—
13	0/9	0/10	+	—	—	0/6	+	0/7	—	0/7	+
14	+	0/7	+	+	+	+	+	0/8	+	0/8	+
15	0/10	0/7	+	0/6	—	0/5	—	0/6	—	0/7	—
16	0/0	0/7	+	0/6	—	0/5	—	0/8	+	0/8	+
17	0/10	0/7	+	0/6	+	0/5	+	0/8	—	0/7	—
18	0/10	0/8	+	0/6	—	0/6	—	0/10	—	0/10	—
19	0/10	0/7	+	0/6	+	0/6	+	0/8	—	0/8	—
				Группа В GROUP							
1	0/10	0/10	6/27	0/6	—	0/6	—	0/6	—	0/6	—
2	0/10	0/10	15/18	0/6	—	0/6	—	0/8	—	0/8	—
3	0/10	0/10	7/25	0/6	+	0/3	—	0/8	—	0/8	—
4	0/10	0/8	16/25	0/6	+	0/6	—	0/8	—	0/8	—
5	0/10	0/10	1/24	0/6	—	0/6	—	0/7	—	0/8	—

LEGEND OF HEADINGS: 1. Strains of the Coxsackie viruses; 2. Initial infection; 3. Cotton rats; 4. White mice; 5. Suckling cotton rats; 6. Silent passage; 7. Cotton rats; 8. White mice; 9. Brain; 10. body (cadaver); 11. Test; 12. Control.

AT BOTTOM OF TABLE: Conventional symbols: numerator . . . number od diseased animals; denominator .... number of infected animals;
- the animal did not get sick;
+ clinically marked sickness with lethal outcome; control anywhere...on suckling white mice.

The character and localization of the changes which the ZhG and NP strains provoked in monkeys are similar to those described in infections with the AB-IV, MK-IV, GZ-IV strains, and with the prototypic strain of Coxsackie A-7.

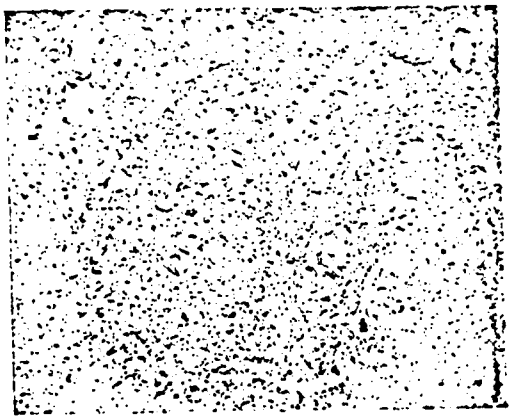


FIGURE 2: Diffuse inflammatory reaction and neuronephagic nodules at the site of dead neural cells in the anterior horn of the spinal cord of a monkey infected with the Coxsackie A-14 virus. Objective 10, Ocular 5. Staining with cresyl-violet by Nissl's method.

The Coxsackie A-14 viral strain does not cause paralysis in monkeys, but their spinal fluid regularly shows pleocytosis with predominance of lymphoid cells. Histological examination confirmed the observation of DALLDORF about the presence of changes in the brain and spinal cord of infected monkeys. The process is similar to the clinical picture caused in certain cases when monkeys are infected with the AB-IV virus, but the changes in the cerebral cortex are much more diffused. In the spinal cord the changes are widely scattered, but larger outfall of neural cells cannot be noticed in any single segment. Evidently, this will also explain the absence of paralysis in monkeys (Fgiure 2). Another peculiarity of the Coxsackie A-14 virus is the presence of histological changes in the brain and muscles of two-week old white mice infected with this virus.

From all other known Coxsackie viruses, the Coxsackie A-9 virus is distinguished by its pathogenicity for white mice. The virus causes lethal disease in white mice at the initial infection, and a passage of the virus could not be made in white mice.

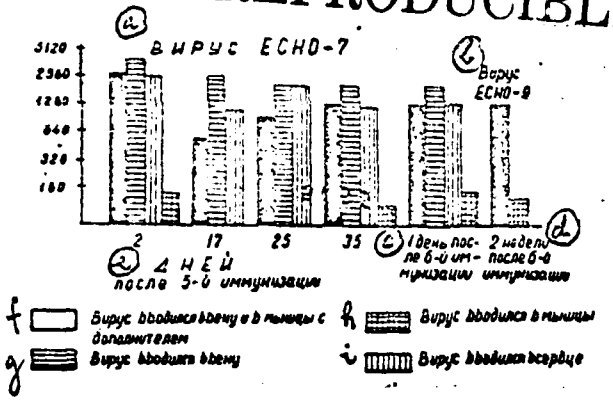
The antigenic activity of the ECHO viruses, when together with the additive they are inoculated into rabbits, is presented in Table 6. The highest activity was shown by the Types 2, 6, 9, 1, 5, 7 and 12 of the ECHO viruses. The titres of immune sera to these viruses were over 1:1000. The Types 8, 18, 11, 13, 15, 3, 14 and 19 of the ECHO viruses possessed less antigenic cavity. Particularly low antibody titres (less than 1:320) were noticed in the immune sera to the ECHO viruses Type 4 and 17.

The greatest antigenic activity was shown by the ECHO-7 virus at intravenous injection (the antibody titre was higher than 1:2560). In regard to antibody titre value, similar results were reached by inoculating the ECHO virus intracardially or in combination with the additive into vein and muscle (Titre 1:2560). When the ECHO-7 and ECHO-9 viruses were injected only into the muscle, the antibody formation was inferior (Figure 3).

TABLE 6: ANTIBODY TITRES TO VIRUSES OF THE ECHO GROUP IN SERA OF IMMUNIZED RABBITS

Типы сывороток к вирусу ECHO (1)	Количество ТЦД (2)	Титр сыворотки к гомологичному вирусу (3)	Титр сыворотки к гетерологичным вирусам ECHO и полиомиелита I, II, III типов (неспецифич. реакция) (4)
2	100	1 : 5120	0
6	100	1 : 2560	0
9	100	1 : 2560	0
1	1000	1 : 1280	ECHO-13 — 1 : 80
5	100	1 : 1280	0
7	100	1 : 1280	5 Полиовирус III типа — 1 : 5
12	100	1 : 1280	0
8	1000	1 : 1060	ECHO-6 — 1 : 20
18	1000	1 : 640	ECHO-6 — 1 : 10
10	100	1 : 512	—
11	100	1 : 640	0
13	100	1 : 500	ECHO-1 — 1 : 80
15	100	1 : 500	0
3	100	1 : 320	6 Полиовирус II типа — 1 : 20
14	100	1 : 320	0
19	100	1 : 320	0
17	100	1 : 160	7 Полиовирус III типа — 1 : 10
4	100	1 : 20	0

(HEADINGS): 1. Serum types to ECHO virus; 2. Amount of TCD_{50} of the virus; 3. Titre of serum to the homologous virus; 4. Titres of serum to heterologous ECHO viruses, and to poliovirus Types I, II, III (non-specific reaction); 5. (in table column 4: Type III poliovirus; 6. (In table column 4: Type II poliovirus; 7. (in table column 4: Type III poliovirus.



(WORDS ON FIGURE:)

a. ECHO-7 virus
b. ECHO-9 virus
c. one day after the sixth immunization
d. 2 weeks after the sixth immunization
e. Δ days after the fifth immunization
f. the virus was introduced into vein and muscle with the additive
g. the virus was introduced into vein
h. the virus was introduced into muscle
i. the virus was inoculated into the heart

FIGURE 3: Relation of the antigenic activity of ECHO-7 and ECHO-9 viruses to the methods of virus inoculation

TABLE 7: TITRES OF ANTIBODIES TO THE COXSACKIE GROUP-A VIRUSES IN IMMUNE SERA OF RABBITS

Type of Coxsackie-A virus	Amount of neutralized viral doses	Titre of serum to the homovirus
1	100	1 : 12800
2	10000	1 : 32000
3	1000	1 : 32000
4	100	1 : 32000
5	1000	1 : 16000
7	10000	1 : 8000
8	1000	1 : 8000
12	100	1 : 8000
6	1000	1 : 4000
10	33	1 : 1600
14	1000	1 : 1000
16	1000	1 : 1000

From the two methods of immunization accepted in working with Coxsackie-A viruses, the first was the most effective, i.e., inoculation of the virus into vein and muscle, and into muscle with the additive. The titres of immune sera with antibodies to A-2, A-3, and A-4 viruses exceeded 1:32,000 when the sera were prepared by the first method (Table 7).

The second method of immunization, which differs from the first so that the virus is not inoculated intramuscularly, was less acceptable. At the immunization of rabbits by the second method, the titres of immune sera were considerably lower, and they did not exceed 1:8000 (A-6, A-7, A-8, A-10, A-12, A-14 and A-16).

CONCLUSIONS

1. The studied viral strains of the ECHO group are non-pathogenic in monkeys, cotton rats, white mice, suckling cotton rats, suckling white mice, guinea pigs and rabbits.

2. Suckling cotton rats are highly sensitive to Coxsackie A viruses which are pathogenic in suckling white mice.

In suckling cotton rats, Coxsackie B viruses will cause affections in an irregular manner, but the viruses can be easily adapted to these animals in the first silent passage.

3. Viruses of the AB-IV-Coxsackie A-7 group and the Coxsackie A-14 virus possess marked myotropic properties in suckling cotton rats and white mice. This is a characteristic feature of each member of the A group. At the same time, in adult cotton rats they provoke paralysis which has the histological picture of experimental poliomyelitis.

4. The PN and GZh strains in the AB-IV - Coxsackie A-7 group caused the clinical picture of experimental poliomyelitis in monkeys when these animals were infected either with the original suspension of fecal matters, or even with a suspension of the spinal cord of infected monkeys. Here the histological changes were similar to those seen in monkeys infected with the AB-IV, MK-IV, GZ-IV and WP strains of Coxsackie A-7.

5. The Coxsackie A-14 virus does not cause paralysis in monkeys and white mice, but at histological examination the brain and spinal cord show distinct inflammatory degenerative changes, similar to the picture of experimental poliomyelitis in monkeys -- still more diffuse in regard to its localization.

6. The Coxsackie A-9 virus causes sickness in adult white mice at the initial infection, but no passage of the virus could be made in these animals.

7. The Types B-1 -- B-5 and A-1 -- A-6, A-10 -- A-12, A-15--A-19 Coxsackie viruses did not cause clinically any marked affection in white mice, cotton rats, guinea pigs, and rabbits.

8. The ECHO virus strains are different in regard to their antigenic capacity in rabbits. The ECHO-7 virus had the highest antigenic activity when injected into a vein.

9. The highest titres of antibodies to Coxsackie viruses were obtained with a combined method of immunization when the virus was inoculated into vein and muscle with the additive.

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