questionable reactions, and the remainder no clot destruction.

Menstruation. Of 18 bloods drawn on the first day of seemingly normal menstruation, 2 showed no lysis, 8 +++, 6 ++++, and 2 dissolved completely.

Miscellaneous. Two patients with abruptio placenta showed ++ lysis, one non-pregnant patient with chronic glomerulonephritis showed +, one child with nephrosis +++, and one pregnant patient with thrombocytopenic purpura +++.

Discussion. The results of the study of this group of patients indicate that fibrinolytic activity is absent in the normally pregnant patient but may be present when certain complications arise. That this ability to destroy clot is not associated with any specific complication is suggested by the fact that it was present in association with a variety of conditions. The fact that fibrinolysis could be demonstrated only in those patients in whom chronic vascular renal disease was associated with proteinuria and edema suggests that this condition closely resembles preeclampsia, in which fibrinolysis is uniformly present. In view of these findings it becomes evident that this test cannot be utilized as a means of accurately differentiating between vascular renal disease and the specific pregnancy toxemias.

15449

Effect of Minerals on Susceptibility of Swiss Mice to Theiler's Virus.*

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The more recent developments in our knowledge of nutrition have made it possible with some species of animals to use diets composed only of highly purified components. As a result it has been possible to study the role of certain specific nutritional factors in susceptibility to infectious diseases. Previous reports from this laboratory[1-3] have concerned the effect of vitamin deficiencies on the resistance of mice and monkeys to experimental poliomyelitis. The general biological importance of calcium, phosphorus, sodium, potassium and other minerals led us to undertake the following experiments on the effect of single deficiencies of these minerals on the susceptibility of Swiss mice to Theiler's GDVII virus.

Methods. The complete synthetic diet was composed of the following parts per 100: sucrose 73, vitamin-free casein 18, salts IV 4, and corn oil 5. The vitamin supplements per 100 g of diet were: thiamine 0.3 mg, riboflavin 0.3 mg, pyridoxine 0.3 mg, niacin 0.5 mg, calcium pantothenate 2.0 mg, *i*-inositol 100 mg, choline 300 mg, *p*-amino benzoic acid 100 mg and biotin 5 μg. The several mineral-deficient diets were produced by supplying the corresponding salt mixture from Table I instead of salts IV at the percentage indicated in that table. The phosphorus-low diet was produced by replacing the casein with blood fibrin and by giving the phosphorus-free salt mixture. All of the mice received distilled water and an adequate amount of oleum percomorphum *per os* each week.

Twenty-one- to 24-day-old Swiss† mice

* These studies were aided by a grant from The National Foundation for Infantile Paralysis, Inc.

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TABLE I.
Composition of Salt Mixtures for Mineral Deficient Rations.* †

	Salts IV	Sodium	Potassium	Calcium	Magnesium	Phosphorus	Chloride
$CaCO_3$	1200	630	475	—	1200	1325	1200
$CaHPO_4$	248	248	1484	—	248	—	248
K_2HPO_4	1290	1290	—	1290	1290	—	1290
$NaH_2PO_4 \cdot H_2O$	—	—	—	200	—	—	—
K_2CO_3	—	—	—	—	—	1020	—
$MgSO_4 \cdot 7H_2O$	408	408	408	408	—	408	408
$NaHSO_4$	—	—	—	—	198	—	—
NaCl	670	—	670	670	670	670	—
Na_2CO_3	—	—	—	—	—	—	615
$CaCl_2 \cdot 2H_2O$	—	830	—	—	—	—	—
$FeC_6H_5O_7 \cdot 5H_2O$	110	110	110	110	110	110	110
KI	3.2	3.2	—	3.2	3.2	3.2	3.2
NaI	—	—	2.9	—	—	—	—
$MnSO_4 \cdot 4H_2O$	20	20	20	20	20	20	20
$CuSO_4 \cdot 5H_2O$	1.2	1.2	1.2	1.2	1.2	1.2	1.2
$ZnCl_2$	1.0	1.0	1.0	1.0	1.0	1.0	—
$ZnSO_4$	—	—	—	—	—	—	1.2
Total (gm)	3951.4	3541.4	3172.1	2703.4	3741.4	3558.4	3896.6
% of salts in ration	4.0	3.6	3.3	2.8	4.0	3.6	4.0
Control ration (addition per kilo)		Na_2CO_3	K_2CO_3	$CaCO_3$	$MgCO_3$	$NH_4H_2PO_4$	NH_4Cl

* All mice received distilled water.
† These salt mixtures were calculated by James H. Shaw.
‡ 15 g of $NH_4H_2PO_4$ supplies 50% more P than the amount in optimum diet. This is necessary to compensate for the amount of phosphorus present in 18% casein but which is not present in fibrin.

bred in our laboratory and split litter technic with consideration for sex and weight were used in all experiments.

The GDVII strain of Theiler's virus[3] was given by intracerebral injection of 0.03 ml in a 1% concentration. Uninoculated mice were maintained on both deficient and optimal diets for control purposes and to determine the most desirable time for virus administration, so that the end of the incubation period in the mouse should occur at the peak of the deficiency. After inoculation the mice were observed twice daily.

Results. Potassium. On this diet with potassium-free salts, young mice failed to grow and developed signs of unkempt fur, general weakness, apathy, extreme inactivity and anorexia. The mice lost 1-1.5 g during the first week and generally maintained this weight up to 21 days, although in some instances additional weight losses up to 1.0 g were recorded. Following this period the mice lost weight rapidly and died during the fourth week.

† Original source was the laboratory of Dr. Webster.

When 5% of the potassium level in salts IV was supplied, the mice lost only 0-1.5 g during the first week but slowly gained up to their initial weights, during the following 2 weeks. These animals developed the same signs as the mice fed diets devoid of potassium, but the mortality rate was considerably lower. When 15% of the potassium level in salts IV was supplied the mice gained up to 5.0 g during the first 14 days, and then either gained weight slowly or maintained their body weight. These mice appeared normal and no deaths occurred in this group. When 30% or 100% of the potassium level in salts IV was supplied the mice gained 3.5-5.0 g per week during the 4-week experimental period and were normal in all respects. A total of 447 mice was employed in potassium studies.

In Table II are presented the data on the percentage of paralyzed animals in the various groups of potassium-deficient mice. Those fed diets devoid of potassium showed a marked resistance to the invasion of this virus (32% paralyzed), but a progressively decreased resistance was seen as the potassium level was increased to the optimal level (91% para-

TABLE II.

Influence of Level of Potassium and Sodium in Diet on Resistance of Swiss Mice to Theiler's GDVII Virus.

Series No.	No. of days on ration	No. of days after inoc.	% of mice paralyzed					Series No.	No. of days on ration	No. of days after inoc.	% of mice paralyzed		
			K def. (34)*	5% of opt. K (35)	15% of opt. K (33)	30% of opt. K	K opt. (34)				Na def. (18)	Na opt. (18)	Na-K def.
57	8	5	0	14	15		26	57	36	7	15	15	
		6	18	26	36		56			8	31	54	
		7	21	37	58		74			9	31	62	
		8	27	46	73		85			10	31	69	
		9	29	51	79		91			12	46	85	
		10	32	51	79		91			14	46	92	
										15	54	92	
			(22)			(30)	(27)				(24)	(26)	(27)
54	13	5	0			3	4	68	30	6	4	27	11
		6	0			13	15			7	30	54	11
		7	0			13	15			8	39	62	11
		8	0			27	48			9	43	65	11
		9	5			47	56			10	69	85	18
		10	5			60	70			13	69	88	18
		11	9			67	78						
		12	14			70	78						
			(19)				(19)						
62	10	6	16				53						
		7	32				68						
		8	32				84						
		9	32				89						
		10	37				95						

* Numerals in parenthesis indicate number of mice inoculated.

TABLE III.
Influence of Level of Phosphorus in Diet on Resistance of Swiss Mice to Theiler's GDVII Virus.

Series No.	No. of days on ration	No. of days after inoculation	% of mice paralyzed: 5% of optimum P (18)*	15% of opt. P (25)	30% of opt. P (24)	opt. (25)
61	15	5	17	8	38	4
		6	17	24	42	12
		7	28	32	46	36
		8	28	36	50	64
		9	33	44	54	72
		10	33	48	58	80
		13	33	48	58	80
			(21)	(19)	(21)	(21)
67	11	5	29	21	19	19
		6	38	26	24	19
		7	43	32	38	43
		8	48	32	48	67
		9	48	37	57	76
		10	48	42	67	86
		11	48	42	67	90
		12	48	42	71	90
		15	48	42	76	90

* Numerals in parenthesis indicate number of mice inoculated.

lyzed). The results clearly indicate that the incidence of paralysis varied directly with the potassium level of the diet.

Sodium. When mice were fed diets containing sodium-free salts they grew poorly and developed rough coats in 2-3 weeks, but were normal in other respects. The average weight gain for the first week was 2.0 g: during the following 3 weeks the animals did not gain and then began to lose weight slowly. There were no deaths in mice receiving this diet until the 6th week at which time the mortality was high. Control animals received diets containing an amount of sodium equivalent to that in salts IV. These animals gained 4.0 g per week and were normal in all respects.

A concomitant deficiency of sodium and potassium was produced by feeding for 21 days a diet containing a salt mixture which was free of sodium and contained only 15% of the potassium supplied by salts IV. After 21 days, all of the potassium was removed from the diet and by 30 days the mice had developed signs of the multiple deficiency of sodium and potassium. These signs were similar to those seen in mice fed potassium-low diets. The addition of potassium at a level of 15% of the optimal was found to be necessary to prevent the high mortality of a potassium deficiency, while producing a sodium deficiency which commonly required about 4 weeks.

Mice fed diets devoid of sodium showed a somewhat lowered incidence of paralysis than control groups which had received adequate amounts of sodium (Table II). However, when mice were fed diets lacking both sodium and potassium they showed a marked resistance to the invasion of this virus. This resistance was comparable to that shown by mice fed diets lacking only potassium (Table II).

Phosphorus. A phosphorus deficiency was produced in mice by feeding a synthetic diet containing a phosphorus-free salt mixture (Table I) and blood fibrin in place of casein. The animals on this diet grew poorly, averaging a gain in weight of 2-4.5 g during the 4-week period with the major portion of this gain in the first 7-10 days. The deficient mice had a flabby appearance, developed unkempt fur, a rapid and shallow type of respiration and a flaccid paralysis of the hind legs which upon gross examination was indistinguishable from poliomyelitis. When this

TABLE IV.
Influence of Calcium, Magnesium and Chlorine in Diet on Resistance of Swiss Mice to Theiler's GDVII Virus.

Days after inoculation	% of mice paralyzed					
	Ca deficient (26)*	Ca optimum (13)	Mg def. (11)	Mg opt. (20)	Cl def. (19)	Cl opt. (14)
4	0	0	27	25	0	0
5	12	7	45	50	0	0
6	25	23	45	70	0	0
7	44	23	63	75	0	0
8	69	69	63	75	0	7
9	75	77	63	75	16	14
10	75	84	63	75	32	29
11	75	84	63	75	68	50
12	75	84	63	75	68	64
13	75	84	63	75	89	71

* Numerals in parenthesis indicate number of mice inoculated.
Ca—Mice on diet 36 days before inoc.
Cl " " " 49 " " "
Mg " " " 20 " " "

diet was modified to contain that amount of phosphorus (as $NH_4H_2PO_4$) supplied by salts IV and casein in the complete diet, it supported excellent growth (3.5-5.1 g per week) and the mice seemed normal in all respects.

When the amount of phosphorus in the diet was less than that supplied by the complete diet, the animals grew in proportion to the amount of phosphorus supplied. The unkempt fur, rapid respiration and flaccid paralysis of the hind legs no longer developed when 5-15% or more of the phosphorus was supplied in the complete diet. As it was impossible to distinguish between paralysis due to phosphorus deficiency and that due to virus invasion, when phosphorus was completely absent from the diet, we found it necessary to add an amount of $NH_4H_2PO_4$ which was equivalent to 5% of the phosphorus level in the complete diet. Under these conditions the mice did not develop an extreme phosphorus deficiency and flaccid paralysis of the hind legs due to phosphorus deficiency was seldom seen, unless the experimental period was extended to 6 weeks.

As the amount of phosphorus was increased, the per cent of paralyzed animals in the groups of mice receiving these diets likewise increased up to 80-90% in mice fed complete diets (Table III).

Calcium. Mice fed calcium-low diets grew slightly below the normal rate for the first week and then gained even more slowly during the following 4-5 weeks, but the only manifest signs of deficiency were unkempt fur and loose stools. Apparently a severe calcium deficiency did not follow when this diet was used.

However, in a small preliminary experiment (Table IV) no difference occurred in the percentage of paralyzed mice between groups maintained on calcium-low and on complete diets.

Magnesium. When a magnesium-free salt mixture was incorporated into an otherwise complete diet and fed to mice, the animals appeared normal and gained 3 g per week, whereas those fed the same diet with added magnesium gained 4-5 g per week over the same 4-week period. A few mice on the deficient diet did show unkempt fur and occasional evidence of peripheral vasodilatation as manifested by red ears.

There was no difference in susceptibility to Theiler's virus between mice fed diets low or adequate in magnesium.

Chlorine. Our complete diet with a chloride-free salt mixture replacing salts IV did not precipitate a chlorine deficiency in mice, even though care was taken to supply the choline requirements (0.3%) as choline in place of choline chloride.

However, the mice on chloride-low and on complete diets were inoculated with Theiler's virus after a 49-day depletion period. Both groups of mice showed the same incidence of

paralysis after administration of the virus (Table IV).

Summary. The influence of the level of 6 common minerals on the susceptibility of Swiss mice to Theiler's GDVII virus has been investigated in more than 1100 animals.

No demonstrable effect on the susceptibility to this infection was found by varying the level of calcium, magnesium or chlorine in the diet, some effect was noted with sodium, while striking results were obtained with potassium and phosphorus.

A progressively decreased resistance was observed as the amount of potassium or of phosphorus was increased in the diets up to the optimal levels.

15450

Influence of Various Pharmacologic Substances on the Emetic Effect of Intravenous Glutamic Acid in Dogs.

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The intravenous administration of amino acid mixtures of protein digests has become a promising method to aid in maintaining nitrogen balance in patients unable to take adequate food by mouth. A side effect, however, which imposes certain practical limitations is the occasional incidence of nausea and vomiting, particularly when the solutions are administered too rapidly. The chief offender was found to be glutamic acid (Madden *et al.*,[1] and Unna and Howe[2]). Aspartic acid has been shown to have a similar effect (Unna and Howe,[2] Madden *et al.*[3]) in dogs. Other reports have described undesirable side reactions when amino acids or protein hydrolysates were infused rapidly in humans. Although glutamic acid was not specifically mentioned, it is highly probable that in many cases it was largely responsible for the emesis.

With the knowledge that glutamic acid is a predominant offender, an attempt has been made to find drugs which will delay or inhibit emesis resulting from the infusion of a pure solution of the natural (*l*+) glutamic acid. Achieving this might materially enhance the clinical application of protein hydrolysates.

Methods. Healthy mongrel dogs maintained on a standard chow diet were used. Food was not withheld until 2 to 3 hours before the experiment. A 5% solution of *l*+ glutamic acid (not neutralized) having a pH of 1.1 was infused intravenously at a rate of 10 mg/kg/min until vomiting occurred. The substance to be tested as an inhibitor of emesis was either injected shortly before and/or during the glutamic acid infusion, or mixed with the solution. In order to establish individual tolerance, each dog was subjected to an infusion with glutamic acid alone, several days before or after the combined use of glutamic acid and the compound investigated. Any animal failing to vomit with glutamic acid alone was eliminated from the series.

Experimental Observations. Data recorded in Table I for *first-run* dogs show that animals given glutamic acid alone vomited when an average of 136 mg/kg had been administered at the relatively rapid rate of 10 mg/kg/min. Animals tested again within a 4- to 6-day period were found to have developed an increased tolerance (Table II). Therefore, in statistical comparison, it was necessary to use results on "first-runs" only. A rest period of 2 weeks to a month was

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