tibody, were protected against intravenous or intracerebral challenge with virulent canine distemper virus, while the contact controls, not receiving measles virus, became ill, and some died. The dogs which had received distemper virus alone developed distemper neutralizing antibody, but developed no measles neutralizing antibody.

1. Adams, J. M., Imagawa, D. T., PROC. SOC. EXP. BIOL. AND MED., 1957, v96, 240.
2. Carlstrom, G., *The Lancet*, 1957, v273, 344.
3. Warren, J., Nadel, M. K., Slater, E., Millian, S. J., *Am. J. Vet. Res.*, 1960, v21, 111.
4. Cabasso, V. J., Kiser, K. H., Stebbins, M. R., PROC. SOC. EXP. BIOL. AND MED., 1959, v101, 227.
5. Cabasso, V. J., Avampato, J. E., Kiser, K. H., Stebbins, M. R., *Bact. Proc.*, 1960, 106.
6. Enders, J. F., Peebles, T. C., PROC. SOC. EXP. BIOL. AND MED., 1954, v86, 277.
7. Gillespie, J. H., Rickard, C. G., *Am. J. Vet. Res.*, 1956, v17, 103.
8. Dunkin, G. W., Laidlaw, P. P., *J. Comp. Path. and Therap.*, 1926, v39, 213.
9. Gorham, J. R., *Am. J. Vet. Res.*, 1957, v18, 691.
10. Schlesinger, R. W., in *Viral and Rickettsial Infections of Man*, 3rd edition, J. B. Lippincott Co., 1959, 145.
11. Riasantzeva, N. E., *J. Microb., Epid. and Immunobiol.*, 1956, v27, 22.
12. Gillespie, J. H., *Cornell Vet.*, 1960, v50, 514.
13. Robson, D. S., Gillespie, J. H., Baker, J. A., *Cornell Vet.*, 1960, v50, 503.

Received September 29, 1960. P.S.E.B.M., 1960, v105.

The Effect of Niacinamide on Cerebral Circulation. (26172)

T. F. HUANG AND C. C. CHAO (Introduced by C. McC. Brooks)
Department of Physiology and Surgery, Medical College, National Taiwan University, Taipei, Taiwan

It has been reported previously(1,2) that niacinamide has no significant effect on cerebral blood flow when given in doses of 50 to 100 mg intravenously. Large doses of the drug (3-5 g, i.v.) have been shown to increase cardiac output in the dog to a remarkable degree(3) and it was thought that there might be an associated increase in cerebral blood flow. Consequently the effects of small and large doses of niacinamide on cerebral circulation were determined to test this hypothesis.

Method. Dogs were anesthetized by pentobarbital 40 mg/kg i.v. Cerebral blood flow was measured by the N_2O method described by Kety and Schmidt(4-6). The sagittal sinus was exposed and punctured by a needle (15 gauge) and connected by polyethylene tubing with a 3-way stopcock, a manometer (1 mm I.D., 45 cm height) and a heparinized sampling syringe(6,7).

As we had no ready made $N_2O(15\%)$-O_2 (21%)-$N_2(64\%)$ mixture we mixed O_2 and N_2O in the ratio of 60 to 40 by a flowmeter. The O_2 content of the mixture was analyzed by a Scholander gas analyzer(8) and it was found that the gases mixed successfully in the desired ratio.

Control blood samples were obtained 15 min. after puncture of the sinus. After another 15 min interval, the drug was injected intravenously in 20 ml of water and 5 to 15 min later blood samples were taken again. The samples were analyzed in a Van Slyke-Neill manometric apparatus by the method of Orcutt and Waters(9). Mean arterial blood pressure (MABP) readings were taken from the femoral artery. O_2 consumption of the brain ($CMRO_2$) was determined by multiplying arteriovenous O_2 difference and cerebral blood flow (CBF). The data were treated by t-test(10).

Results. The effect of large doses of niacinamide (350 mg/kg) on cerebral circulation in 7 dogs 5-15 min after injection is shown in Table I. CBF/100 g/min increased significantly from 39.4 $\pm$ 7.2 (mean $\pm$ s.e.) to 56.2 $\pm$ 12.0 ml ($P<.01$), and $CMRO_2$/100 g/min. from 2.71 $\pm$ 0.85 to 4.18 $\pm$ 1.47 ml ($P<.05$), while MABP decreased from 139.3 $\pm$ 22.3 to 95.0 $\pm$ 16.6 mm Hg ($P<.001$)

TABLE I. Effect of Large Doses of Niacinamide on Cerebral Circulation.

No. of dogs	Sex	Body wt, kg	Dose of niacinamide, mg/kg i.v.	Cerebral blood flow, ml/100 g/min. (CBF)	Sagittal sinus pressure, mm H_2O	Mean arterial blood pressure, mm Hg (MABP)	Cerebral vascular resistance (CVR)	Cerebral O_2 consumption, ml/100 g/min. ($CMRO_2$)
1	♂	14.0	357	(34.3) 46.8*	(48) 55	(155) 120	(4.54) 2.56	— —
2	♂	10.0	350	(48.8) 89.5	(28) 20	(140) 110	(2.86) 1.23	
3	♀	8.5	375	(53.5) 72.5	(285) 325	(150) 100	(2.76) 1.38	(3.37) 5.80
4	♀	9.0	333	(25.0) 28.0	(400) 200	(125) 55	(5.00) 1.96	(1.95) 2.54
5	♀	9.0	333	(36.2) 51.3	(250) 315	(120) 85	(3.32) 1.66	— —
6	♀	10.0	400	(31.2) 39.0	(195) 250	(160) 95	(5.10) 2.43	(2.56) 3.54
7	♀	10.0	300	(46.5) 66.0	(60) 75	(125) 100	(2.68) 1.52	(2.94) 4.85
Mean ± S.E.		10.1 ± 1.6	349.7 ± 55.2	(39.4 ± 7.2) 56.2 ± 12.0	(180.9 ± 61.2) 177.1 ± 55.1	(139.3 ± 22.3) 95.0 ± 16.6	(3.75 ± .71) 1.82 ± .34	(2.71 ± .85) 4.18 ± 1.41
t				3.566	.108	6.646	7.423	3.586
p				<.01	>.9	<.001	<.001	<.05

* The values with and without parentheses were obtained before and 5-15 min. after administration of the drug respectively.

and CVR from 3.75 ± 0.71 to 1.82 ± 0.34 ($P<.001$). However, sinus pressure showed no change.

In contrast with the above mentioned results, the effect of this drug was quite different when small doses (300-500 mg in total) were administered intravenously in 5 dogs. In this series, CBF, sagittal venous pressure, MABP, CVR and $CMRO_2$ showed almost no influence with small doses of this drug.

Discussion. This experiment clearly shows that niacinamide in large doses had distinct effects on CBF, MABP, CVR and MRO_2 of the brain, while no effect could be observed when small doses were administered. Therefore we agree with other investigators(1,2) that this drug in small doses has no effect on cerebral circulation.

Hosoya *et al.*(11) observed that niacinamide in doses of 500 mg orally administered improved dark adaptation (rod adaptation). Although the mechanism of this effect is not clear, it seems not to be due to an increase in cerebral or retinal blood flow, because the dosage of this drug used by these investigators does not increase cerebral blood flow.

Increase in cardiac output does not necessarily cause increase in regional blood flow. This statement can be supported in the case of epinephrine(12); increase in cardiac output by epinephrine results in an increase in liver, skeletal muscle and brain blood flow, but decreases blood flow in the kidney and coronary artery. Niacinamide in large doses, as shown in this experiment, raised cerebral blood flow; therefore, the effect of this drug on cerebral blood flow paralleled its effect on cardiac output. The mechanism of increase in cerebral blood flow caused by large doses of this drug was thought to be by an increase in cardiac output associated with a decrease in cerebral vascular resistance. The low toxicity of this drug should permit its use to increase brain blood flow and metabolism.

Summary. Niacinamide in large doses (3-5 g) administered intravenously increased significantly cerebral blood flow and cerebral oxygen consumption, but decreased mean arterial blood pressure and cerebral vascular resistance in dogs. This drug in small doses had no such effects. The increase in cerebral blood flow was attributed to an increase in cardiac output associated with a decrease in cerebral vascular resistance.

1. Aizawa, T., *Proc. 15th Gen. Assem. Jap. Med. Congr.*, 1959, v4, 355.

2. Aring, C. D., Ryder, H. W., Roseman, E., Roseman, M., Rosenbaum, M., Ferris, E. B., Jr., *Arch. Neurol. Psychiat.*, 1941, v46, 649.

3. Huang, T. F., *Am. J. Physiol.,* 1959, v196, 735.
4. Kety, S. S., Schmidt, C. F., *ibid.,* 1945, v143, 53.
5. Kety, S. S., in V. R. Potter, *Method in Medical Research,* The Year Book Publisher, Inc., 1948, v1, 204.
6. Kety, S. S., Schmidt, C. F., *J. Clin. Invest.,* 1948, v27, 476.
7. Bering, E. A., Jr., *Am. J. Physiol.,* 1959, v197, 825.
8. Scholander, P. F., *J. Biol. Chem.,* 1947, v167, 235.
9. Orcutt, F. S., Waters, R. M., *ibid.,* 1937, v117, 509.
10. Snedecor, G. W., *Statistical Methods,* Ames, Iowa State College Press, 1940.
11. Hosoya, Y., Fang, H. S., Peng, M. T., *Tohoku J. Exp. Med.,* 1950, v53, 103.
12. Grollman, A., *Pharmacology and Therapeutics,* Lea Febiger, 1960, 4th ed., 277.

Received September 30, 1960. P.S.E.B.M., 1960, v105.

Adaptation of Coxsackie Virus Strain A-10 to Human Amnion Cells in Tissue Culture.* (26173)

T. H. DUNNEBACKE AND C. F. T. MATTERN† (Introduced by W. M. Stanley)
Virus Laboratory, University of California, Berkeley

Following the purification of poliovirus(1) and Coxsackie virus A-10(2), an effort has been made to compare a number of properties of these 2 enteroviruses. Much is known about the biology of the polioviruses, but since Coxsackie virus A-10 could be grown only in suckling mice it was impossible to make a comparative study of the biological behavior of these physically similar viruses. Therefore, attempts were made to adapt Coxsackie virus A-10 to tissue culture. Coxsackie virus A-10 was inoculated onto cultures of cells of human origin (primary amnion(3), HeLa, FL cells(4), and amnion strains A_1-A_7(5)). It was found that the virus multiplied in and caused a cytopathic change in the cells in the primary human amnion cultures but not in the cells of the other cultures tested.

A sample of highly purified, suckling mouse grown Coxsackie virus A-10 was diluted in medium 199 containing 20% lamb serum and sterilized by filtration through a Seitz pad. The sterile filtrate was further diluted to have a titer of about 8.4×10^7 suckling mouse LD_{50} per plate of cells, or about 50-100 LD_{50} per cell.

The virus inoculum was placed on 8 petri plates, 4 from each of 2 different preparations of primary human amnion cells (A-847, A-852). Two additional plates from each amnion preparation served as controls and contained only medium 199 with 20% lamb serum.

The control and the inoculated plates were observed daily, and on days 1, 3, 6 and 10, one inoculated plate from each cell preparation was removed from the incubator. The supernatant medium was removed and frozen; the cells on the plates were washed with phosphate buffer, fixed in Bouin's fluid, and stained with haematoxylin. Additional medium (4 ml 199-20% lamb serum) was added to the remaining plates on day 5. Control plates were sampled on days 6 and 10.

On days 1 through 6, no noticeable difference between control and inoculated cells was observed either before fixation or after fixation and staining. On the 8th day, the inoculated plates appeared to differ somewhat from controls, and by the 10th day they were grossly cytopathic. The cells on the control plates appeared to be healthy and well-maintained at 10 days.

The supernatant fluid from each of the 10-day inoculated cultures was diluted 1:5, and each was placed on 2 plates of amnion preparation A-856. The cells of A-856 were grossly cytopathic 3 days after inoculation with the supernatants of both A-847 and A-

* Aided by Am. Cancer Soc. grant E-82.

† Present address: Lab. of Biology of Viruses, Nat. Inst. of Allergy and Infect. Dis., N. I. H., Bethesda, Md.