oil pouches and dermis, but incorporation into the purines of nucleic acids from either of these tissues is unaffected. The data here reported do show some variation in response, which might possibly be accounted for by individual animal variations. It is interesting to note, however, that in croton oil pouch protein residues, the activity of the tissue is directly proportional to the weight of the pouch. Where the weight is high, as in the control tissues, specific activity is also high. One control tissue which, for some unknown reason, did not respond to the croton oil injection, showed lower radioactive glycine incorporation, similar to the incorporation found in test pouches.

To evaluate its specific role in connective tissue metabolism, we have attempted to determine whether BAPN acts primarily on regulation of cellular uptake or utilization of amino acids in collagen synthesis. Since glycine uptake into acid insoluble purines is unaltered by feeding BAPN, it would appear that BAPN does not exert its effect at the level of nucleic acid synthesis in the cellular component of the connective tissue. On the other hand, the observed lowering of glycine incorporation into the protein residue is compatible with earlier findings indicating an inhibitory action of BAPN on the synthesis of extracellular collagen by these same cells.

Summary. 1. An investigation of the influence of BAPN on incorporation of glycine-1-C^{14} into proteins and nucleic acids of rat croton oil pouches and dermis was undertaken. 2. Incorporation of glycine into protein residues of fibrous tissue from croton oil pouches was decreased about 25% in animals pretreated with BAPN. In protein residues of dermis the rate of incorporation of glycine was also decreased, but to a much lesser degree, about 15%. 3. Studies of the nucleic acid fraction indicate that no change occurs in glycine uptake in fibrous tissue of dermis or croton oil pouches from BAPN treated animals as compared to controls. 4. The results of these experiments suggest that BAPN primarily affects amino acid incorporation into collagen or ground substance rather than the cellular portion of connective tissue.

1. Dasler, W., *Fed. Proc.*, 1954, v13, 519.
2. Ponseti, I. V., and Shepard, R. S., *ibid.*, 1954, v13, 473.
3. Bachhuber, T. E., Lalich, J. J., Angevine, D. M., Schilling, E. D., and Strong, F. M., PROC. SOC. EXP. BIOL. AND MED., 1955, v89, 294.
4. Mielke, J. E., Lalich, J. J., and Angevine, D. M., *ibid.*, 1957, v94, 673.
5. Selye, H., *ibid.*, 1953, v82, 328.
6. LePage, G. A., *Cancer Res.*, 1953, v13, 178.
7. Markham, R., and Smitth, J. D., *Biochem. J.*, 1950, v46, 509.
8. ———, *ibid.*, 1951, v49, 401.

Received July 22, 1957. P.S.E.B.M., 1957, v96.

Thresholds for Pain and Convulsions in the Guinea Pig Following Massive Whole-body Irradiation. (23473)

HOWARD L. ANDREWS (Introduced by Falconer Smith)
Department of Health, Education and Welfare, P.H.S., Nat. Cancer Inst., Radiation Branch, Bethesda, Md.

The guinea pig shows an abrupt shortening of survival time and a striking change in mode of death(1) when a single whole-body radiation dose exceeds 6,000 r (6 Kr). Below 6 Kr the clinical picture is essentially that of depression, while above 6 Kr excitation, with frequent convulsions, is regularly seen. Pentobarbital sodium, given prior to radiation, prevents the clinical signs of excitation(2) and lengthens survival time. The observable neuropathology(3) appears insufficient to account for the early death and this suggested the present study on the functional state of some accessible neurological systems.

Previous studies(4) have shown only small and subtle effects on the electroencephalogram at doses below 6 Kr and paroxysmal seizure waves at higher doses. Changes in the elec-

TABLE I. Convulsive Thresholds.

Radiation (Kr)	Milliamperes avg* at various times (hr)							Avg survival (hr)
	Pre r	*4–6*	*24–29*	*48*	*72*	*144*	*168*	
5	20	20	19	23	22	25	23	158
		.2	*1*	*6*				
10	22	15	4	2				12
		28	*49*	*75*				
10†	19	17	22	18				121

* Each value is avg of 2 to 4 animals.
† Pentobarbital sodium (35 mg/kg) i.p. preceded radiation exposure.

trocardiogram are small except when the animal is moribund. One of the more prominent features of the high-dose syndrome is the hypothermia which appears early and may persist until death. Gerstner *et al.*(5) reported a rise in pinna reflex threshold 3 hours after 8 Kr to the head. Twenty-four hours after irradiation the pinna reflex was abolished. We have obtained essentially similar results with the pinna reflex but have experienced difficulty in obtaining consistent responses. The present report concerns convulsive thresholds as elicited by electric shock and "pain threshold" determined by reaction to thermal radiation. Sharp end points and reproducible responses can be obtained with both of these reactions.

Methods. Adult male guinea pigs (800-1200 g) from the NIH hybrid stock were used. All radiations were delivered with a Van de Graaff generator operating at 2.5 Mev, TSD 75 or 100 cm, dose rate 500-2,000 r/min., HVL 10 mm lead. All doses were administered by an integrating ionization chamber circuit, calibrated before each run against a thimble chamber. Electric shocks were delivered through electrodes clipped to the ears after washing with acetone and vigorously applying conducting electrode paste. Stimuli of 3 sec. duration were delivered by a motor driven switch. The stimulus consisted of a 60 cycle alternating current supplied by a transformer through a high series resistance which reduced the effect of varying electrode resistance. Current was measured by the voltage drop across a standard resistor. Convulsive threshold was taken as that current required to produce a convulsion with both tonic and clonic components. Current was varied in steps of about 2.5 milliamperes and no attempt was made to obtain readings closer than this. Below-threshold stimuli were spaced at least 15 minutes apart to prevent summation. "Pain threshold" measurements used essentially the procedure(6) developed for the dog. Radiation from a 750 watt projection bulb was focussed onto the shaved, blackened skin of the back. Three-second stimuli were repeated at 30-second intervals. Threshold was taken as the watts input to the lamp needed to elicit a characteristic muscular twitch(7). This may not be a response to pain but it is at least closely related and involves a large segment of the nervous system.

Results. Table I shows the results of convulsive threshold measurements in animals receiving 5 Kr, 10 Kr, and 10 Kr preceded by 35 mg/kg pentobarbital sodium, i.p. In the latter group post-radiation measurements were not made until several hours after each animal had returned to an apparently normal state of alertness.

The 10 Kr data shown in Table I were taken when no spontaneous convulsions were occurring. Handling incidental to electrode placement did not elicit convulsions but after 10 Kr these were always produced at the lowest current value tested. From this fact, and the length and severity of the induced seizures it seems probable that the 10 Kr post-r values may be somewhat lower than those given. It did not seem worthwhile to establish more exact values.

As Table I shows, the drop in threshold at 10 Kr occurs rapidly but is not coincident with absorption of the radiation. Threshold values were nearly normal in 2 animals tested 12 minutes after the mid-point of a 10 Kr, 10 min irradiation, but at 1 hour each unmedicated animal had a low value.

Table II gives the results of the pain

TABLE II. Pain Thresholds.

Radiation (Kr)	Watts avg* at various times (hr)								Avg survival (hr)
	Pre r	*1*	*24*	*96*	*120*	*144*			
5	176	181	179	173	186	196			147
		.5	*5*						
10	169	170	191						12
		.1	*2*	*24*	*-48*	*+48*	*139*	*163*	
5 + 5,† 48 hr later	177	194	169	158	184	233	244	220	156

* Each value is avg of 4 animals except at 139, 144 and 163 hr where only 3, 3, and 1 animals, respectively, were surviving.

† Time measured from the first of 2 exposures.

threshold measurements.

Pain-threshold data from animals receiving a single dose of 5 Kr show no significant trends although there was a tendency toward somewhat higher values a few hours before death. Data obtained from animals receiving 10 Kr and pentobarbital were similar to those from 5 Kr animals and have been omitted from Table II. The 10 Kr data at 5 hours are presented as found but are of dubious value because almost continuous muscle twitching obscured the sharp end points usually obtained.

Divided dose experiments have been done with intervals between irradiations ranging from 2 to 48 hours. The large, prompt increase in threshold shown in Table II was seen only at the longest interval. A small prompt increase was seen when the doses were spaced 19 hours apart but at shorter intervals no prompt effect of the second dose was evident.

Discussion. The convulsive threshold data confirm what would have been inferred from clinical observations, and emphasize the differences existing between guinea pigs receiving less than, or more than, 6 Kr whole-body radiation. The suppression of clinical signs of convulsions by pentobarbital undoubtedly results from its ability to prevent the sharp drop in threshold usually seen after 6 Kr or more. At 5 Kr there is no significant trend in the pain threshold data although the values tend to rise as the animal becomes moribund. The abrupt, prompt rise in threshold observed after a second 5 Kr dose appears much like a sensitivity reaction. The high values observed with the divided dose schedule are not approached at any time with a single 5 Kr dose. Observations following 10 Kr are difficult, but it appears that here also pain threshold values are lower than those seen with the 2 doses spaced 48 hours apart.

The relative constancy of the pain threshold response indicates that function is relatively unimpaired in a large portion of the nervous system. The responses obtained may not represent true pain thresholds but certainly afferent and efferent fibers are involved and thalamic integration and cortical localization of response seems to be required. The hypothalamic areas probably responsible for the observed hypothermia, and the cerebellar areas showing pyknotic cells are presumably not involved in the reactions studied here.

Summary. Pain thresholds were tested using the thermal radiation from a projection bulb as a stimulus, and convulsive thresholds to electric shock were determined with ear electrodes. Radiation doses of 5,000 r and 10,000 r were used to bracket the critical 6,000 r dose, above which signs of nervous system injury predominate. Pain thresholds remained relatively constant at each radiation dose until the animals became moribund. Convulsive thresholds were relatively constant at a dose of 5,000 r but dropped sharply following 10,000 r. Pentobarbital given prior to 10,000 r prevented the drop in convulsive threshold even after the obvious drug effects had disappeared. The essential constancy of the pain threshold response indicates that function is relatively unimpaired in a large portion of the nervous system.

1. Brace, K. C., Andrews, H. L., and Thompson, E. C., *Am. J. Physiol.*, 1954, v179, 386.

2. Andrews, H. L., and Brace, K. C., *ibid.*, 1956, v187, 378.

3. Alvord, E. C., and Brace, K. C., *J. Neuropath. and Exp. Neurol.*, 1957, v16, 3.

4. Andrews, H. L., and Brace, K. C., *Am. J. Physiol.*, 1953, v175, 138.

5. Gerstner, H. B., Konecci, E. B., and Taylor, W. F., *NP* (4856) *Rep.* 8, Sept. 1953.

6. Andrews, H. L., and Workman, W., *J. Pharmacol. and Exp. Ther.*, 1941, v73, 99.

7. Winder, C. V., *Yale J. Biol. and Med.*, 1947, v19, 289.

Received July 22, 1957. P.S.E.B.M., 1957, v96.

Neonatal Immunity. I. Disparity in Maternal-Infant Poliovirus Antibody.* (23474)

MURRAY M. LIPTON AND ALEX J. STEIGMAN

Kentucky Child Health Fn. Laboratory, Department of Pediatrics, University of Louisville School of Medicine, Louisville, Ky.

The studies here reported concern the titers of poliovirus antibodies to the 3 serotypes in the serum of mothers and their newborn infants. It represents part of a study on the local formation and transfer of antibody *in utero*. Since we are dealing exclusively with infants at the moment of birth, the possible role of colostrum will not be discussed nor will the uncertain role of the placenta in production of antibodies. The subject of active and passive immunity of the infant has been reviewed by Edsall(1). Previous reviews include one on placental permeability by Doerr (2). One of the earliest observations of antibody transfer in the human from mother to infant concerned that of diphtheria in 1895 (3). Later studies demonstrated transmission of tetanus antibodies(4). More recently, however, the concern has been with the quantitative aspects of maternal transmission of antibody and, therefore, neonatal immunity.

Although one might expect all antibodies to behave similarly with respect to maternal-infant transmission, this does not appear to be the case. Reagins reportedly do not appear in the umbilical serum whereas blocking antibodies do(5). Viruses may differ among themselves in this respect, thus in Japanese B encephalitis(6) and mumps(7) no disparities have been observed whereas they have been found in vaccinia(8). Employing untyped poliovirus in qualitative tests in monkeys, Aycock and Kramer reported neutralizing antibody in 10 of 12 matched maternal-cord serums tested(9). Among the 3 serotypes of polioviruses we have observed disparities in titer most marked in Type 3. Rather than stress the anticipated agreements we have chosen to consider the possible meaning of the observed disparities among the 3 serotypes.

Methods. A series of 48 mothers' and corresponding umbilical cord bloods were collected aseptically generally at term; this includes 4 prematures and 3 sets of twins. The immunization record of each mother in regard to poliomyelitis was recorded but not known at the time of antibody titration. Mothers were of various ages, color, and previous obstetrical history who were seen in pre-natal clinics and delivered at a city hospital. The antibody titrations were performed *in vitro* by a modification of the technic originally published by Salk, Youngner and Ward(10). Monkey kidney cells were obtained by seeding bottles with trypsinized monkey kidney tissue. After 1 week the cells were harvested by use of versene and used in a suspended cell neutralization test using 2% calf serum, 0.5% lactalbumin hydrolysate in Hanks' BBS. Twenty thousand cells were used/tube. The matched maternal and umbilical cord serums were always titrated simultaneously, dilutions of both being made by the same worker. For antibody titrations versus each virus type, 100 TCD_{50} of poliovirus either type 1 (Mahoney), type 2 (MEF_1), or type 3 (Saukett)

* This investigation was supported by research grant from Natl. Inst. of Allergy and Infect. Dis., U.S.P.H.S.