in both flexor and extensor prases, and there is no evidence of automatic resumption of reciprocal innervation. Association of the biceps with the extensors does not by itself produce dissociation from the flexors. Only after a further practice period of individually varying duration, does the transplant begin to be omitted during flexor actions.

Even then, however, temporary relapses into the old flexor association occur repeatedly, even years after the operation. These relapses seem to be favored by fatigue, lack of concentration, automaticity of movement, etc. Their occurrence supports the view that the adjusted use of the transplant is not based on the substitution of a permanent extensor association for its former flexor association in the elementary motor mechanisms, but rather on the development in higher centers of a new type of action which can effectively override the innate coördinative associations without abolishing them. This corroborates the distinction between lower, rigid, and higher, plastic systems in the control of coördination suggested by earlier observations.[2]

These and numerous other facts still under examination (the fate of stretch reflexes; action of motor units; differential fatigue) exemplify the advancement of theoretical insight and practical knowledge concerning coördination which physiologists and orthopedic surgeons alike may expect to result from the electromyographic study of transplanted muscles in man.

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Protection in White Mice With Human Convalescent Serum Against Infection With Poliomyelitis Virus (Armstrong Strain)*†

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The results reported in this communication are the outcome of an

2 Weiss, P., and Ruch, T. C., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 569.

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

† The human convalescent serum used in these experiments was obtained from patients of the Walnut Street School for Crippled Children, in Lansing, Michigan, and of the Blodgett Convalescent Home, in Grand Rapids, Michigan. To both the donors and to the staffs of these institutions and the many others who made the collection of the blood possible the author wishes to express his deepest appreciation.

attempt to reëvaluate the *in vivo* action of human convalescent serum, utilizing Swiss mice infected with the Armstrong strain of poliomyelitis virus.

At the moment human convalescent serum is in disrepute as a therapeutic or prophylactic agent. There is little to be gained in reviewing the many pros[1] and cons[2] regarding its effectiveness since it was first used in the treatment of the human disease in 1911.[3] It might perhaps suffice to say that its use appeared rational, since human convalescent serum possesses the property of neutralizing potent suspensions of monkey adapted virus.

Attempts to establish the usefulness of convalescent serum as a prophylactic and therapeutic agent in the experimental disease in the monkey have been equally inconclusive. The most complete study testing its prophylactic value was carried out by Schultz and Gebhardt.[4] These authors reported suggestive protection in monkeys against small infective doses of virus following the administration of large doses of highly potent immune horse and convalescent human and monkey serums. Our own continued attempts[5] to modify the disease in the monkey by the administration of large doses of human convalescent serum (10-20 cc per pound body weight) following infection, have been negative. The infectivity of the cords of those treated animals likewise appeared unmodified.

It has long been recognized, however, that there have been serious limitations to the use of the monkey as the experimental animal. The successful transmission by Dr. Charles Armstrong of the National Institute of Health[6] of a monkey strain of poliomyelitis virus to the cotton rat and white mouse has supplied an effective tool.

Experience with the Armstrong strain during the past 20 months,

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1 *a.* Aycock, W. L., and Luther, E. H., *J. A. M. A.*, 1928, **91**, 387; *b.* Aycock, W. L., Luther, E. H., McKhann, C. F., Smith, E. C., and Kramer, S. D., *J. Infect. Dis.*, 1929, **45**, 175; *c.* Levinson, S. O., McDougall, C., and Thalhimer, W., *J. A. M. A.*, 1932, **99**, 1058; *d.* McKenzie, M., *Canad. M. A. J.*, 1929, **21**, 291; *e.* Brebner, W. B., Preliminary Report of the Results of the Administration of Normal Adult Serum in the Prophylaxis of Poliomyelitis During the 1932 Epidemic, Poliomyelitis, Williams & Wilkins Co., 1932, p. 529; *f.* Stokes, J., Jr., Wolman, I. J., Carpenter, H. C., and Margolis, J., *Am. J. Dis. Child.*, 1935, **50**, 581.

2 *a.* Kramer, S. D., Aycock, W. L., Solomon, C. I., and Thenebe, C. L., *New Eng. J. Med.*, 1932, **206**, 432; *b.* Park, W. H., *J. A. M. A.*, 1932, **99**, 1050.

3 Netter, A., Gendron, and Touraine, *Compt. rend. Soc. de biol.*, 1911, **70**, 625, 707, 739.

4 Schultz, E. W., and Gebhardt, L. P., *J. Ped.*, 1935, **7**, 332.

5 Kramer, S. D., unpublished.

6 *a.* Armstrong, C., *Pub. Health Rep.*, 1939, **54**, 1719; *b.* Armstrong, C., *Pub. Health Rep.*, 1939, **54**, 2302.

which has included a clinical and pathological study of this strain in monkeys, as well as in rats and mice, and a comparison by means of cross protection tests with at least 3 other strains of virus, leads us to concur with others[7] in the belief that this is a strain of poliomyelitis virus.

Experimental. Strain of Virus and Virus Dilutions. The strain of virus kindly supplied to us by Dr. Charles Armstrong was employed throughout these experiments. Since August, 1940, this strain has remained quite constant in potency. Three 10-fold dilutions of the virus were employed (5%, 0.5%, and 0.05%) in all but Experiments XVI and XVII.

Route of Infection. Infection was accomplished by the intracerebral inoculation of 0.03 cc of the virus suspension into the left cortex.

Incubation Period. This has varied with the concentration of infecting dose employed. In general the correlation between dose of virus and incubation period has followed the pattern described by Sven Gard, as it applies to infection with viruses by the intracerebral route.[8]

Animals. Three-week-old Swiss mice averaging 10 g in weight were employed throughout the experiments. Eight mice were used for each dilution (except in Experiments XVI and XVII). When a mouse died within a few hours following inoculation, it was subtracted from the total number.

Controls. Comparable numbers of control animals were simultaneously infected in each experiment. The control animals received either no serum or normal monkey serum (see charts).

Source of Serum and Method of Administration. The serum used in all but Experiment I came from a single pool of 13 donors. All donors had had the disease within 2 years and showed residual paralysis. A neutralization test was done on each serum and those possessing good neutralizing power were pooled. The pools were filtered, tested for sterility, and bottled without preservative.

The serum (human convalescent and normal monkey) was administered by the intraperitoneal route. Details of the administration of the serum with regard to amount, frequency, and time in relation to infection are indicated in each of the experiments in Charts 1 to 4 inclusive.

Two additional experiments (not illustrated in the charts) were

[7] *a.* Rivers, T. M., *Infantile Paralysis, 1941,* published by the National Foundation for Infantile Paralysis, Inc., p. 60; *b.* Harford, C. G., and Bronfenbrenner, J., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 211.

[8] Gard, S., *J. Exp. Med.*, 1940, **72**, 69.

CHARTS 1-4.

In Vivo Protection in White Mice with Human Convalescent Serum Administered Intraperitoneally Against Intracerebral Infection with Poliomyelitis Virus (Arm strong Strain).

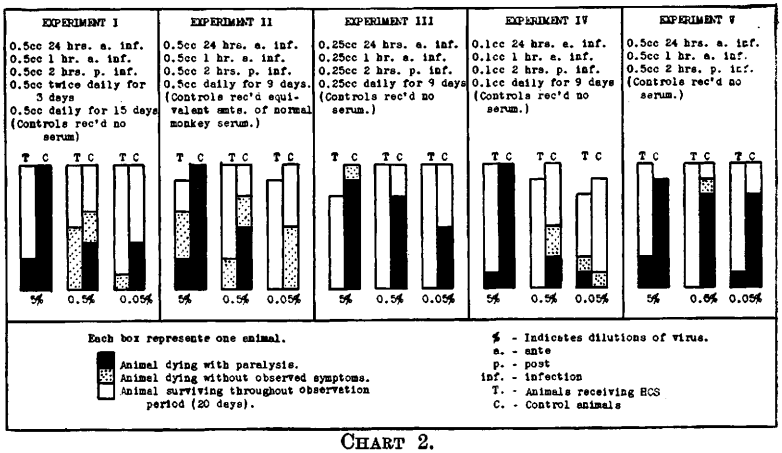


CHART 2.

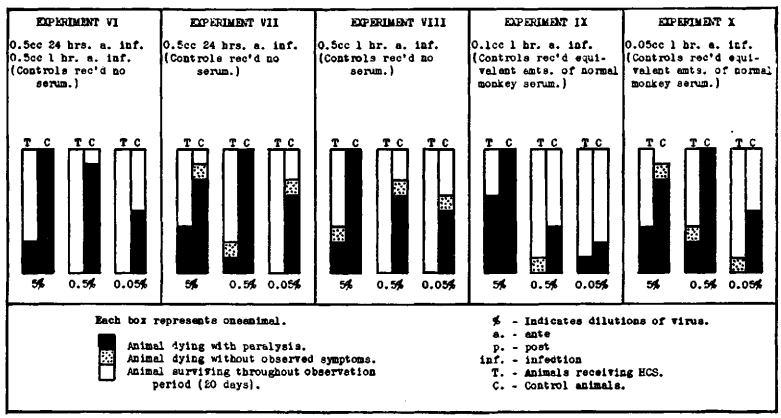


CHART 3.

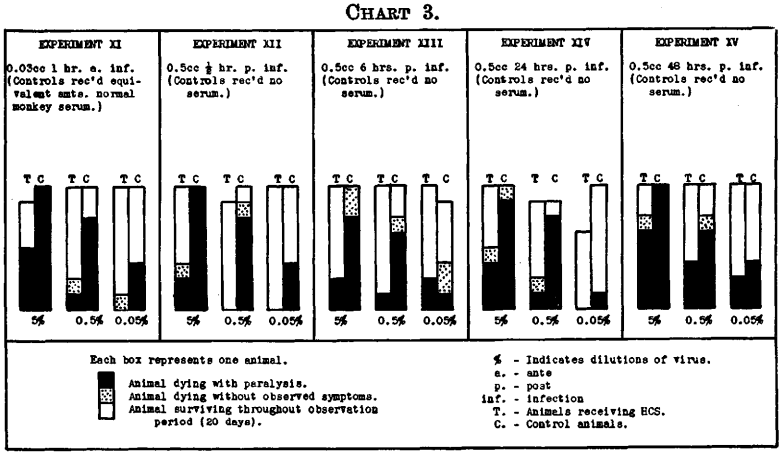
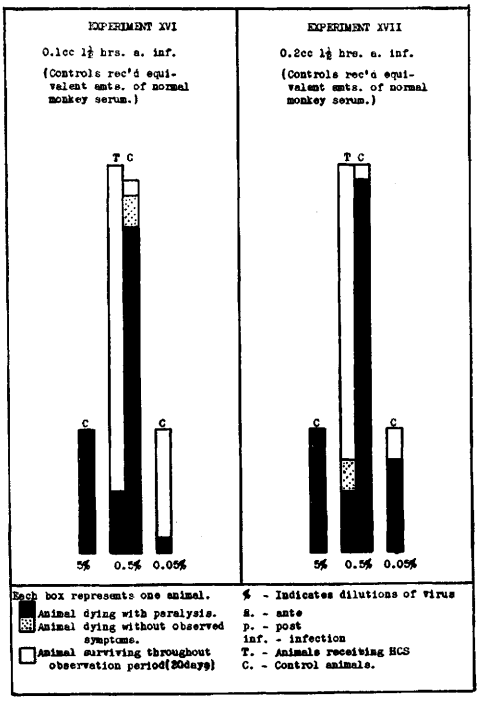


CHART 4.



conducted, in which immune globulin‡ was used in place of human convalescent serum. The dosage, method and frequency of administration were essentially the same as used in Experiment I.

Results. From the results of Experiments I and II, two things of possible significance stand out. When 0.5 cc of human convalescent serum is administered with the frequency and time with relation to infection indicated in the chart, significant protection is apparent in both experiments. This is also apparent in Experiments III and IV, in which the dose of serum administered was reduced to 0.25 and 0.1 cc respectively. Comparable though not as striking protection was obtained in the 2 experiments in which immune human globulin was administered in place of convalescent serum. The second point of significance (not illustrated in these charts) was the failure of the continued use of serum or immune globulin to modify the illness. Animals which contracted the disease did so within the normal incubation period and these animals lived no longer than did control animals developing the disease; in both groups, treated and control, such animals died from one to 5 days after the onset of symptoms.

‡ Kindly supplied by Lederle Laboratories.

In Experiments V, VI, VII, and VIII, the individual dose of serum was maintained at 0.5 cc but the total quantity administered and the time with relation to infection was varied. Protection is apparent in all 4 experiments, even when a single dose of 0.5 cc was administered 24 hours before infection.

In Experiments IX, X, XI, single doses of convalescent serum but in varying amounts were administered to the treated group of animals one hour before infection. The results indicate that appreciable protection resulted even when 0.03 cc of serum was administered; although protection was not as apparent as when 0.5 cc of serum was employed (Experiment VIII).

In Experiments XVI and XVII (Chart 4), 0.1 cc and 0.2 cc respectively of convalescent serum was administered 1½ hours before infection. The more critical middle dilution was selected as the infecting dose of virus. Twenty-five mice were placed in each of these groups with comparable numbers of controls. A smaller group of control untreated mice (8 mice for each of the other 2 dilutions) was included as a check on the titration of the virus. The results appear clearcut; significant protection was obtained in the animals receiving the convalescent serum over the controls which had received equivalent amounts of normal monkey serum.

In Experiments XII, XIII, XIV, and XV (Chart 3), an effort was made to determine whether or not protection could be obtained if the convalescent serum was administered after infection. Significant protection was obtained when the serum was administered ½, 6 and 24 hours, but not 48 hours, after infection.

Summary. This report is based on 19 completed experiments designed to reëvaluate the usefulness of human convalescent serum.

From these experiments it would appear that it is possible to protect a significant number of 3-week, 10 g mice against intracerebral inoculation of poliomyelitis virus (Armstrong strain) by the intraperitoneal administration of from 0.03 to 0.5 cc of potent human convalescent serum—protection being somewhat more evident in those mice receiving larger doses of serum. Evidence of protection is furthermore obtained when the serum is administered up to 24 but not 48 hours after intracerebral infection.

Under the experimental conditions there appears to be no evidence that convalescent serum had any therapeutic effect, even when this was administered continuously from 24 hours prior to infection to 9-15 days following infection. Animals that succumbed to the disease did so within the usual incubation period and died, as did the controls, from one to five days after the onset of paralysis.

No attempt is or can be made at this time to translate the results of these experiments in terms appropriate for human application. They are reported, however, because we believe they represent the first definite evidence of significant protection with human convalescent serum under the experimental conditions.

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Electrical Rectification in Single Nerve Fibers.

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The electrical resistance of an ordinary conductor is independent of the magnitude or direction of a current sent through it, and a current may pass with equal ease in either direction. There have been suggestions, however, that in a nerve fiber membrane, current may pass more easily in one direction than in the other, or that the nerve fiber membrane behaves as a rectifier rather than a simple resistance.

Recently, Cole and Baker,[1] and Cole and Curtis[2] demonstrated rectification in the squid axon, using alternating current bridge methods and the needle electrode technic. Another paper, Cole,[3] shows that the previous failure of Cole and Hodgkin[4] to observe rectification in this axon was due to the fact that only small currents had been used and to the fact that the effect under the anode was approximately equal and opposite to the effect under the cathode, thus neutralizing it.

By killing one end of the nerve fiber, neutralization of rectification under one electrode by that under the other can be avoided, and it should be possible to observe rectification directly by means of a much simpler technic involving a direct current Wheatstone bridge.

The giant nerve fiber of the hindmost stellar nerve of the squid, *Loligo pealii,* was used throughout the experiments. It was care-

1 Cole, K. S., and Baker, R. F., *J. Gen. Physiol.*, 1941, **24**, 535.

2 Cole, K. S., and Curtis, H. J., *J. Gen. Physiol.*, 1941, **24**, 551.

3 Cole, K. S., *J. Gen. Physiol.*, 1941, **25**, 29.

4 Cole, K. S., and Hodgkin, A. L., *J. Gen. Physiol.*, 1939, **22**, 671.