three to four days and no manifestations of adrenal insufficiency appeared.

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THE ENCEPHALITOGENIC PROPERTY OF HERPES VIRUS[1]

MODIFICATIONS have recently been reported in the virulence of the viruses of human influenza,[2] vaccinia,[3,4] infectious bronchitis of fowls[5] and pseudorabies,[6,7] following cultivation on the chorio-allantois of chick embryos. This communication is to describe an increase in virulence for chick embryos and a reduction in virulence for rabbits which have occurred in a neurotropic strain of herpes simplex (HF, Rockefeller Institute) during 70 serial passages on the chorio-allantois of chick embryos. The technique of establishing and maintaining membranal strains of viruses has been described elsewhere.[8]

The original HF virus on membranes metastasized rarely to the heart and brain. After the twentieth passage it regularly induced metastatic lesions in the heart, liver, lungs, spleen and kidneys of embryos. Lesions in the heart, liver and spleen are grossly visible areas of necrosis. By subinoculation of membranes, embryonic blood was shown to contain virus at 24, 48, 72 and 96 hours. There was no localization of virus in the brain from the blood stream. The lethal effect of infection has increased so that at the 75th passage embryos rarely survived 96 hours, whereas at the tenth, most embryos survived infection 6 or 7 days.

As virulence for chick embryos has increased, it has diminished for the rabbit. After the 25th passage the membranal strain no longer induced a typical keratitis in rabbits. Fifteen rabbits scarified and inoculated on the cornea at intervals between the 25th and 65th membranal generations have shown only slight lacrimation, mild inflammation of conjunctiva without suppuration, no elevation of temperature and no symptoms of encephalitis. This is in contrast to an invariably fatal encephalitis which follows a suppurative keratitis induced by the original strain.

To determine whether or not this modified virus traveled along the fifth nerve from the cornea to the brain without causing encephalitis, two rabbits were inoculated on their right corneas: one with the 50th membranal generation, the other with HF. Corneal reactions typical of each strain developed. The rabbits were killed at 96 hours. The right Gasserian ganglion and brain at the entrance of the fifth nerve were removed from each animal and inoculated onto membranes. Herpes virus transmissible in series was recovered from both the Gasserian ganglion and the brain of the HF control rabbit. Virus could not be demonstrated grossly or microscopically on membranes inoculated with material from the rabbit with the modified virus. This experiment was repeated with the same result using rabbits inoculated with the 53rd generation virus and sacrificed at 96 hours and at 7 days. Material from the medulla of one of these rabbits inoculated intracerebrally into another rabbit induced no symptom.

These experiments led to the conclusion that the HF strain of herpes virus had lost its ability to invade the central nervous system following corneal inoculation in rabbits. A second series of passages through 30 generations over a period of 6 months has not induced a similar modification. Modification of the first strain was observed at the 25th generation 11 months after initiation of the chick strain. Whether the already established modification is a repeatable *Dauermodification* induced by prolonged passage of the virus on chick embryos or a suddenly appearing mutation remains to be determined.

To test the virulence of the modified strain following intracerebral inoculation, suspensions of HF virus (1st membranal generation) and the 62nd membranal generation in dilutions of 10^{-3}, 10^{-4} and 10^{-5} were inoculated intracerebrally into rabbits. All 3 rabbits receiving HF virus died within 5 days of herpetic encephalitis. Each rabbit receiving the modified virus had a remarkably delayed elevation of temperature. One (10^{-4}) is alive 60 days after inoculation; one (10^{-3}) died on the 20th day, and the other (10^{-5}) died on the 26th day.

Preliminary experiments indicate that corneal inoculation with the modified strain induces a stable degree of immunity to HF inoculated on the cornea.

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[1] Aided by a grant from the John and Mary R. Markle Foundation.

[2] F. M. Burnet, *Brit. Jour. Exp. Path.*, 17: 283, 1936.
[3] C. Levaditi, *et al.*, *Revue d'Immunologie*, 4: 481, 1938.
[4] L. Molina, *Zbl. f. Bakt., I. Orig.*, 139: 493, 1937.
[5] F. R. Beaudette (personal communication).
[6] F. M. Burnet, Dora Lush and A. V. Jackson, *Aust. Jour. Exp. Biol. and Med. Sc.*, 17: 35, 1939.
[7] R. E. Glover, *Brit. Jour. Exp. Path. and Med.*, 20: 150, 1939.
[8] E. W. Goodpasture and G. J. Buddingh, *Am. Jour. Hyg.*, 21: 319, 1935.

THE CHEMICAL COMPOSITION OF SUCKLEYA SUCKLEYANA

FOLLOWING the discovery of hydrocyanic acid in *Suckleya suckleyana* during 1937, together with the experimental work which proved its toxicity to cattle, sheep, rabbits and guinea pigs, the etiology of many of the heretofore unexplained losses in cattle and sheep in eastern Colorado was explained.[1]

[1] Frank Thorp, Jr., A. W. Deem, H. D. Harrington and J. W. Tobiska, *Colo. Exp. Sta. Tech. Bul.*, 22: 1–19, 1937.

This seemed a desirable plant in which to study the factors influencing HCN formation. The chemical composition of *Suckleya suckleyana* and its relation to the toxic properties of the plant is an important physiological problem.[2]

Preliminary studies of the carbohydrate and nitrogen content of poison Suckleya showed the soluble carbohydrates to be chiefly reducing sugars which varied from one per cent. in seedlings to 2.5 per cent. in three-months-old plants. The sucrose content never exceeded 0.25 per cent. at any stage of development studied.

The starch content showed only moderate variation from early June to August.

Close relationship was found between the HCN and reducing sugar content. The HCN varied from a minimum of 0.018 per cent. at the time of minimum sugar content to a maximum of 0.240 per cent. when the sugar was highest.

Young plants contained a higher percentage of protein or colloidal nitrogen than old plants, but the older plants were higher in soluble nitrogen.

The marked reduction of protein nitrogen with advance of the season, accompanied by an equally rapid formation of HCN, is a behavior worthy of further investigation which may help to clarify some of the problems of nitrogen metabolism in plants. It is probable that following the exhaustion of available nitrates from the soil, synthesized proteins may be digested and the nitrogen constituent of the molecule then used in the formation of glucosides which yield HCN upon hydrolysis.

The data showed no accumulation of starch during the period of protein nitrogen diminution but rapid increase of reducing sugars. This relationship between the hexose sugars, colloidal nitrogen, soluble nitrogen and HCN suggests that the presence of available carbohydrates may stimulate the synthesis of the HCN—containing glucoside. The above relationship also suggests that this synthesis probably is not checked by limited nitrates, providing factors have been favorable for liberal protein formation in the early part of the season.

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EXPERIMENTAL CHRONIC CADMIUM POISONING[1]

CONTINUED feeding of albino rats with an adequate diet to which cadmium as the chloride had been added has been conducted in this laboratory for the purpose of studying the toxicity of chronically ingested cadmium. The details of this study will be reported elsewhere, but three symptoms of toxicity are so striking and of such importance as to justify a preliminary announcement in addition to the report presented at the twenty-third annual meeting of the Pacific Division of the American Association for the Advancement of Science.

The concentrations of cadmium added to the basic diet were 0.0031, 0.0062, 0.0125, 0.025 and 0.05 per cent. The symptoms of toxicity observed were bleaching of the enamel of the incisor teeth, anemia, and cardiac hypertrophy. The bleaching of the teeth is similar to, if not identical with, that produced by fluorides, and occurred on all dosage levels of cadmium. The degree of bleaching was proportional to the dosage. The anemia was likewise present on all dosage levels of cadmium, the severity increasing with the percentage of cadmium added to the diet. The cardiac hypertrophy was most evident on cadmium concentrations of 0.0062, 0.0125, and 0.025, and less evident on a concentration of 0.05 because the rats died before the hypertrophy could fully develop. Since the cardiac hypertrophy was not limited to the left ventricle, it is believed that the anemia rather than hypertension resulting from kidney damage was the causative factor.

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[1] Food Research Division Contribution No. 455.

[2] A paper presented at the Virginia meeting of the American Society of Plant Physiologists.

BOOKS RECEIVED

HENDRICK, IVES. *Facts and Theories of Psychoanalysis.* Second edition, revised. Pp. xiv + 369 + xv. Knopf. $3.00.

HERZBERG, GERHARD. *Molecular Spectra and Molecular Structure; I, Diatomic Molecules.* Pp. xxviii + 592. 181 figures. Prentice-Hall. $6.50.

Palao Tropical Biological Station Studies, No. 4; A List of the Fishes of the Palao Islands, and Other Papers. Pp. 523–694. Illustrated. Japan Society for the Promotion of Scientific Research, Tokyo.

Texas Agricultural Experiment Station: Fifty-first Annual Report, 1938. Pp. 281. Agricultural and Mechanical College of Texas.

University of Illinois Bulletin; Papers Presented at the Fifth Short Course in Coal Utilization, Held at the University of Illinois, May, 1939. Pp. 173. Illustrated. The University. $0.50.

Vitamin E. A Symposium Held Under the Auspices of the Food Group (Nutrition Panel) of the Society of Chemical Industry, April, 1939, at the School of Hygiene and Tropical Medicine, London. Pp. viii + 88. The Society. 5/–.

Zoologica; Scientific Contributions of the New York Zoological Society. Pp. 265–384. Illustrated. The Society.