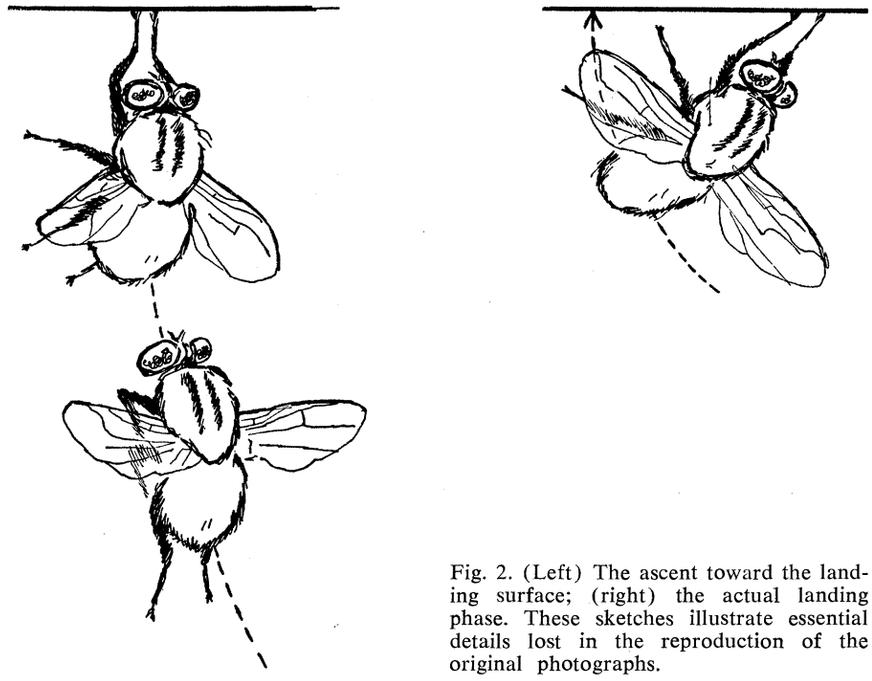

Fig. 2. (Left) The ascent toward the landing surface; (right) the actual landing phase. These sketches illustrate essential details lost in the reproduction of the original photographs.

foot rolls of film were exposed, and one confirming record of a landing maneuver was obtained.

Analysis of all the films exposed to date by the methods outlined reveals that the landing maneuver is essentially comprised of two phases: (i) the ascension, or approach, and (ii) the actual landing operation. The general mechanics of the approach are quite clear in the photographs. In each case the fly ascended toward the ceiling in a near-vertical flight path at a typical velocity of 25 cm/sec. The frequency of wingbeat varied between 144 and 240 cy/sec. A large supination twist of the wings at the beginning and at the end of the downstroke provided the required thrust for vertical climbing. When the fly approached within about a body's length of the ceiling, all its legs were extended outward—the forelegs reaching forward. Continued vertical motion head-on into the ceiling brought the two forefeet into contact with the landing surface with sufficient momentum (¼ gcm/sec) to firmly attach the pulvilli and to aid in the execution of phase ii of the landing maneuver. With its forefeet firmly bound to the landing surface, the fly swung its body forward sufficiently to bring its other legs into contact with the surface. Independent fluttering of the wings served to stabilize the body during this movement. The origin of the forward torque required to swing the body upward is not entirely clear in the photographs, but the probable components are vertical momentum, centrifugal force resulting from an inside-loop approach path, and wing movement (see Fig. 2).

Some variations in the landing maneuver were observed. In one case the fly went into a rolling movement immediately before "touching down" with its forefeet. The final phase of the maneuver resembled a sidewise handspring or "cartwheel" in which the other four feet were brought into contact with the landing surface. This variation probably accounts for the "half roll" interpretation reported by Eyles (*2*). Qualitatively our findings agree with those of Curran (*3*), who did not report any quantitative data.

Neither the exposing flash nor the nature of the landing surface appear to have any marked effect upon the general mechanics of landing, as recorded by the camera.

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27 February 1962

Staggerer, a New Mutation in the Mouse Affecting the Cerebellum

Abstract. The "staggerer" mutant is recognized by its staggering gait, mild tremor, hypotonia, and small size. Symptoms develop during postnatal weeks 1 to 4 and remain stationary thereafter. The cerebellar cortex is grossly underdeveloped, with too few granule cells and unaligned Purkinje cells. Genetic linkage studies and neuropathological findings distinguish staggerer from other known mutants.

Several dozen independent mutations are known to affect neurological function in mice (*1*). These mutants are potentially of great value for the study of brain structure and development and for the analysis and therapy of neurological disease. However, they are unlikely to be used extensively for these purposes until the phenotypes are defined more fully. In almost no instance has there been a description of pathology which accounts for the clinical neurological findings. We recently recognized a gross brain lesion in a hitherto undescribed mutant and correlated the clinical and neuropathological features.

The mutation occurred spontaneously in a stock of obese mice at the Jackson Memorial Laboratory in 1955. The parents were normal in appearance. The segregation data given later in this report prove the mutation to have been due to a single recessive gene. Clinically the mutation somewhat resembles reeler (*rl*) (*2*), and the name "staggerer," symbol *sg*, is suggested (*3*).

The staggerer mutant mouse is first distinguishable from normal littermates between postnatal days 8 and 12. Of 20 affected animals in seven successive litters, three were detected with certainty on postnatal day 8, five on day 9, two on day 10, two on day 11, and eight on day 12. The mutants are identified most readily in the second postnatal week by their abnormal gait, which is more shuffling and hesitant than the gait of normal littermates. Forward progress is interrupted every few steps by a lurching motion to one side or the other. The mutants remain stationary more of the time than the normal mice, and a mild unsustained tremor sometimes accompanies the initiation of motor activity. At rest the hind limbs often are held abducted and everted about 45 degrees. Sometimes the mutants walk backward with hind limbs splayed outward. Of the mutant mice observed, about 50 percent weighed

less than any normal littermate on the first day of clinical detection and all were lighter than littermates by postnatal day 19.

During the third week the impairment of gait and balance appears more pronounced, particularly in contrast to the increasing motor facility of the normal littermates. The staggerers sometimes fall sidewards even from a sitting position. When walking they hold their trunks close to the ground and tend to drag their tails. A forward-pitching motion now sometimes precedes the staggering. At rest, the trunk and limbs are relatively flaccid, and the examiner can easily push the mouse around with his finger. Hearing and vestibular function are present. The mice swim adequately; even when submerged in water they quickly return to the surface and manage to stay afloat.

During the fourth week some affected mice tend to hold their hind limbs extended and somewhat stiff, even when walking. A few show spastic weakness of the hind limbs. More than 50 percent of the mutant animals died in the fourth week, at about weaning time. Those that survived showed little or no further progression of symptoms but remained lighter in weight than their littermates. Only one homozygous staggerer male has bred. Two clinically abnormal females, presumed to be homozygous staggerers, also produced several litters, but their genotypes were not established beyond doubt, as the offspring did not survive long enough to be classified.

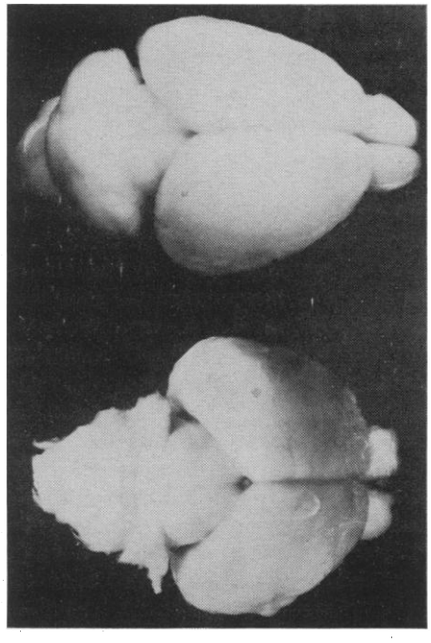

Fig. 1. Dorsal view of brain (top) in a 26-day-old normal mouse and (bottom) in a staggerer littermate. The cerebellum in staggerer is small and lacks normal shape and pattern of folia. [About × 3¼]

In staggerer mutants the cerebellum is so severely affected that the lesion is easily recognized by gross inspection. In adult staggerers the cerebellum is less than one-third normal size and appears as a bar of tissue with few fissures (Fig. 1), somewhat like the cerebellum of a newborn mouse. The abnormality was recognized by postnatal day 4 on the basis of smaller size and less prominent fissure pattern, but was not detected at birth. Histologically the cerebellum of adult staggerers shows tiny folia with shallow fissures and indistinct lamination of the cortical gray matter (Fig. 2). The granular layer is poor in cells, and the molecular layer is thin. The number of Purkinje cells per unit volume of cortex appears to be relatively high, and Purkinje cells are scattered among the granule cells, whereas they form a single row in the normal cerebellar cortex. The external granular layer disappears at about day 15 in control mice (*4*) but persists beyond day 20 in staggerers. Neurons of the dentate and other roof nuclei are relatively numerous and normal looking, as are the myelinated fibers of the cerebellar white matter. Adult reeler mice also have small cerebella, but the histological appearance is different (*5*). Also, unlike staggerer, reeler has extensive disease elsewhere in the brain (*6*).

The pathological findings in staggerer are predominantly or exclusively those of a cerebellar cortical disease manifested soon after birth. Most of the clinical signs also reflect cerebellar disease. Although the pathology is grossly evident at 4 days of age, the clinical features do not appear until the second postnatal week, when the normal mouse develops effective cerebellar control of gait and stance and staggerer does not. Almost all the clinical signs become evident within the first few postnatal weeks, the major period of histogenesis in the cerebellar cortex (*4*). Thereafter the disease is stationary.

Ninety-three offspring were raised from the original heterozygous staggerer parents: 75 normal mice and 18 staggerers. This ratio does not differ significantly ($X^2 = 1.580$) from the expected 3:1 for a single recessive gene. In addition, one homozygous staggerer male bred when outcrossed to a strain C57BL/6J female and sired a litter of eight. All eight offspring were normal in appearance, and each produced *sgsg* progeny when mated *inter se*. The F_2 progeny consisted of 108 normal mice and 28 staggerers, a close approximation to the expected 3:1 ratio ($X^2 = 1.4117$). These data prove that the condition is caused by a single recessive gene.

Animals known to be heterozygous for staggerer (*sg*+) were mated with animals known to be heterozygous for ataxia (*ax*+), jittery (*ji*+), reeler (*rl*+), and ducky (*du*+), and a minimum of 16 offspring were classified for each cross. No abnormal offspring were produced in any of the crosses. This sug-

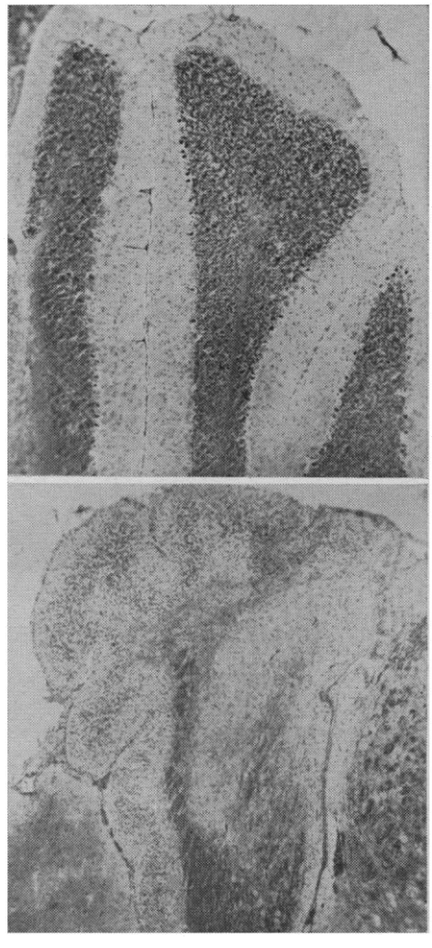

Fig. 2. Transverse section of lateral cerebellar cortex (top) in a 20-day-old normal mouse and (bottom) in a staggerer littermate. One folium of the cortex in the section of the normal cerebellum occupies almost the same area as the whole cerebellar hemisphere in staggerer. Luxol fast blue hematoxylin stain was used. [About × 45½]

gests that staggerer is not identical to, or allelic with, any of these genes.

Linkage tests have been made with five dominant marker genes—*Ra, Os, Mi^{wh}, W^v*, and *T*. The intercross data from the offspring of the fertile staggerer male, plus information from additional breeding tests, provide linkage data for the nonagouti (*a*) and brown (*b*) loci. No close linkage was found with any of these markers, but the recombination with W^v (35.81 ± 9.62), while not significantly different from ½, suggests that more data may reveal a significant linkage. Since *rl* is known to be about 29 units from W^v (*7*), additional tests for allelism between *sg* and *rl* and more linkage tests with marker genes in this linkage group (III) will be made.

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Polyoma and Papilloma Viruses: Do They Have 42 or 92 Subunits?

On the basis of a number of similar properties exhibited by rabbit and human papilloma viruses, polyoma virus, and SV_{40} (vacuolating agent), Melnick (*1*) has suggested grouping these viruses as "papova" viruses types 1 to 4, respectively. The similarities included the appearance of 42 morphological subunits (capsomeres) on the surface of these four viruses. Before these observations of 42 morphological subunits become established criteria for the classification of these viruses, it would seem worthwhile to reconsider the evidence upon which these observations are based.

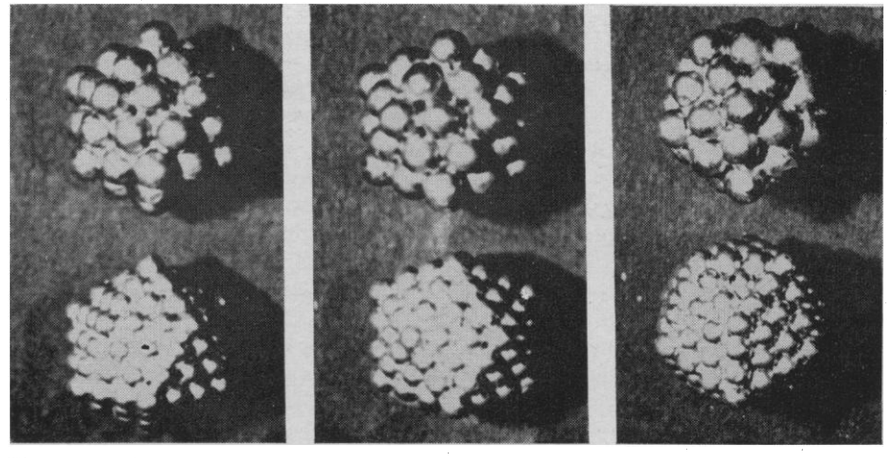

Fig. 1. Icosahedral models constructed of 42 (upper) and 92 (lower) spheres, seen from left to right on 3-, 2-, and 5-fold rotation axes.

Wildy *et al.* (*2*), Howatson (*3*), and Howatson *et al.* (*4*) have interpreted the subunit orientation of polyoma virus and human papilloma virus, respectively, as being of 5 : 3 : 2 symmetry and consisting of 42 morphological subunits, presumably in the configuration of an icosahedron having six shared subunits on each of 20 faces. The studies of Williams *et al.* (*5*) on the Shope papilloma virus indicated that about 30 subunits were visible on about half of the virus particle or "something like 60 knobs on the surface of the entire virus particle." The evidence for 42 subunits on SV_{40}, (*1*) is unconvincing on the basis of published micrographs.

Problems in the interpretation of electron micrographs of viruses negatively stained with phosphotungstic acid (PTA) have been discussed (*5, 6*). On the basis of these discussions and the evidence presented below, it seems at least equally possible that these viruses contain 92 rather than 42 morphological subunits.

In most of the micrographs under consideration there is evidence of obscuring of the virus periphery by a halo of phosphotungstic acid. Williams *et al.* (*5*) clearly demonstrated a decrease in the apparent diameter of the Shope papilloma virus with increasing thickness of the imbedding phosphotungstic acid and an apparent decrease in diameter of PTA-stained particles compared to metal shadowed viruses. Similar obscuring of the edges of tobacco mosaic virus by phosphotungstic acid has been described (*6*). The center-to-center spacing of rods of tobacco mosaic virus in close packing has been well established by x-ray diffraction and microscopy of metal shadowed particles to be 150A. The same spacing is observed between rods imbedded in phosphotungstic acid, but the apparent width of these particles is frequently as small as 120A. It is likely that most negatively stained virus particles are obscured peripherally to a greater or lesser extent. Furthermore, the observation of some 30 subunits on about half of the papilloma virus (*5*) may imply that there are substantially more than 60 subunits on the entire virus surface since one would not expect to resolve clearly those subunits lying in planes which are very nearly perpendicular to the supporting grid.

Models containing 42 and 92 spheres in icosahedral orientation are presented in Fig. 1. They are seen along 3-, 2-, and 5-fold rotation axes, which order corresponds to the decreasing probability of observing viruses of similar shape since they would be in planar, linear, and point contact, respectively, with the grid. The model consisting of 42 subunits would, in all likelihood, present no more than 12 peripheral subunits when viewed on 3- or 2-fold axes and no more than 10 subunits when seen along a 5-fold axis. Most of the virus particles in the studies in question clearly show considerably more than 12 subunits on their periphery. In those particles in which subunits cannot be resolved around the entire periphery, six subunits may be frequently observed on approximately a third of their periphery. This appearance is compatible with the 92 subunit model in which one might see 18 peripheral units