ence can be drawn because of the small number initially present. In numerous other experiments, however, where killing by penicillin was less extreme, the number found after exposure to penicillin was reduced to about the same extent as the total viable count. This is reasonable in view of the equivalent growth rates of normal and *R* cells in nutrient broth.

The disproportionate survival of *D* variants when the total viable count is reduced by penicillin could conceivably be an artifact if for any reason the number of *D* colonies appearing in implants from a given culture was not proportional to the number of viable cells in the implants, when no penicillin had been used. Peculiar effects of this kind were noted by Barer (*6*). To rule out such a possibility, control experiments were performed in which diluted (1 : 20) and undiluted implants from the same culture were plated onto *SM* agar. The number of *D* (and *R*) colonies from the diluted implants was consistently about 5% of the number from undiluted implants. This shows that when no differential bactericidal effect is operative, the number of *D* colonies obtained from a given culture is approximately proportional to the viable count of the implant.

To show that the original small inoculum used contained no cells capable of growth on *SM*, several implants of more than 300,000 cells were made on *SM* agar. As these yielded no growth whatever, it can be confidently stated ($P < 0.002$) that the inoculum of 600 cells in the experiment of Table 1 contained no *R* or *D* cells, and that both these variants must have arisen during growth of the broth culture.

The findings reported here provide clear-cut evidence that a normal bacterial population is inhomogeneous from the standpoint of the ability to give rise to *SM*-dependent colonies on implantation onto *SM* agar. The number of *D* colonies appearing is approximately proportional to the total viable count of the implant under normal conditions, *but not when the culture has been exposed to penicillin.* After such exposure the number of *D* colonies decreases much less than the total viable count. The simplest and most satisfactory explanation of the inhomogeneity, consistent with what is known about the preferential action of penicillin upon actively growing cells, is that *SM*-dependent organisms are themselves present in a normal population before contact with *SM*. Such cells may be presumed to arise by spontaneous mutation, and may be thought of as lethal mutants which will only survive and multiply if transferred to a *SM*-containing medium. Their relative insensitivity to penicillin would result from their poor growth in the absence of the specific growth requirement, and the position would be analogous to that of the various biochemically deficient mutants. The only alternative explanation would be that precursors of *D* cells are present in a normal population, that these are relatively insensitive to penicillin, and that they only give rise to *SM*-dependent clones by some adaptive process after transfer to a *SM* medium. If slow growth were especially favorable to adaptation, the *D* precursors might be those cells in the normal population that grow most slowly and are therefore also relatively insensitive to penicillin. Experiments now in progress are designed to distinguish between these two alternatives.

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Cocontraction and Reciprocal Innervation in Voluntary Movement in Man

Milton G. Levine and Herman Kabat

Kabat-Kaiser Institute, Vallejo, California

The coordination of muscular activity in voluntary movement involves a number of neuromuscular phenomena, one of the most important of which is the alternate action of antagonistic muscles. It has been a seemingly empirical observation known to many that antagonists cease to function when agonist muscles begin to contract. A simple example of this is the relationship of the triceps and the biceps in alternate flexion and extension of the elbow. When the elbow is flexed, the triceps is relatively inactive; when the elbow is extended, the biceps is quiet. There is no doubting the observation. However, there has been a gross oversimplification of the nature of its causation and its actual occurrence under all conditions of muscular contraction.

The most commonly accepted thesis in regard to the interrelationship of antagonistic muscles states that the contraction of a muscle produces by proprioceptive action a central inhibitory effect on its antagonist muscle. This hypothesis is based on the huge body of excellent work reported by Sherrington (*1*) in a series of classic papers. The inhibitory effect upon the skeletal muscles is not brought about through specific inhibitory nerves such as the vagus when it causes cardiac inhibition or the sympathetic nerves which cause inhibition of contraction of the intestinal muscles. Direct stimulation of motor nerves to the skeletal muscles results only in excitation. The inhibitory process is, therefore, considered to be central in origin. Stimulation of proprioceptive end organs in the contracting muscle is thought to cause cessation or diminution of excitatory impulses along the motoneuron to the antagonist muscle.

The alternate inhibition and stimulation of contraction in antagonistic muscles was labeled by Sherrington as reciprocal innervation. Innumerable experiments performed by him and by later observers substantiated the existence of this phenomenon. However, most of the observations were made with decerebrate or spinal animals or animals under anesthesia, in all

of which voluntary control was eliminated. There was a minimum of observations on actual voluntary movement. Sherrington did, however, perform a few indecisive experiments with this in mind; for example:

> I have watched with interest in Macacus the voluntary movements of the eyes after section of the 3rd and 4th nerves. In the early hours after the section, if, for instance, these nerves have been cut on the left side only, the gaze is readily directed to the left but not so readily to the right. There arises, of course, considerable external squint of the left eye. Neither when the right is directed toward the right nor when it is converged upon a light or other object just in front of the face is there more than a mere trace of movement of the left eye. Twenty-four or forty-eight hours later, when the right eye is turned to right, the left eye does perform the conjugate movement, but imperfectly and also more variably than under experimental excitation of the frontal cortex.

The close relation of the innumerable observations made under the special conditions of animal experimentation without voluntary control are not applicable without qualification to voluntary movement, especially in man. As a matter of fact, Sherrington himself pointed out that antagonists may be in contraction concurrently. This he attributed to *double* reciprocal innervation, "in which the balance between inhibition and excitation is such as to allow both half-centers to discharge, although unequally." He believed inhibition to be not only a suppressor of reflexes but a "delicate adjustor of the intensity of reflex contraction." Here again the emphasis is on reflex rather than voluntary contraction, and Sherrington himself would probably decry the oversimplification of the phenomenon as stated in a current text on physical medicine (*2*): "Reciprocal innervation means that when a voluntary or reflex contraction occurs, as in the biceps muscle, it is accompanied by relaxation of its antagonist, the triceps muscle."

Actually, as early as 1925 Tilney and Pike (*3*), in a comprehensive study, concluded that under normal conditions they were unable to observe Sherrington's phenomenon. Rather, they concluded, "muscular coordination depends primarily on the synchronous cocontractive relation in the antagonist muscle groups." Wachholder (*4*) demonstrated cocontraction in the human in a very interesting experiment. By alternately flexing and extending the elbow, he showed that when the alternate movements were performed "loosely" there was apparently no potential generated by the antagonist, but as the movements were "stiffened," cocontraction of the antagonist increased. He concluded that "reciprocal innervation of the antagonist and voluntary motion are therefore reconcilable." Actually, participation of the antagonist in the performance of it must be pointed out again that inactivity of the antagonists is not synonymous with inhibition. The apparent contradiction between Sherrington's findings in the reflex state and the observations of Tilney and Pike may be resolved if we take into account the influence of volition as a modifier of the reflex state. Observations which are true for the reflex no longer hold when volition is introduced; there is a tremendous body of work to back up such an assertion.

Our own interest in the rehabilitation of patients with neuromuscular disease has necessitated the clarification of this question. The understanding of the role of cocontraction and/or reciprocal innervation is essential not only for understanding the dynamics of normal voluntary motion in man, but also for the understanding and treatment of paralysis associated with neuromuscular disease.

Muscular antagonism must be looked upon as a relative phenomenon. Only muscles acting on single joints can be assumed to be true antagonists. Muscles acting on more than one joint may at times act as antagonists and at other times as synergists. The rectus femoris is the antagonist of the hamstring muscles at the knee, but it also helps flex the hip, so by simultaneously flexing the hip and the knee we may observe that the rectus femoris now is acting synergistically with the hamstrings. Furthermore, some muscles which functionally are considered as homogeneous are actually anatomically not so; and as a result, depending on the particular movement, one part of the muscle may act as an antagonist and another part as a synergist. The triceps is such a muscle. It has three points of origin; the lateral and medial heads arise from the humerus, whereas the long head arises from the scapula. In spite of its multiple origins, the triceps is usually listed as an extensor of the elbow joint. It does act in this capacity when the elbow is extended; however, the long head also produces extension and adduction at the shoulder, and cocontraction may occur between the biceps and the long head of the triceps if the shoulder is extended or adducted during flexion of the elbow.

Even in pure single joint antagonism, the inhibition of the antagonist is a relative matter which depends primarily on the number of motor units involved in the contraction of the agonist. In unresisted voluntary movement, there is no doubt but that the antagonist is inactive while the agonist is in contraction, but, as resistance to agonist contraction is applied, the antag-

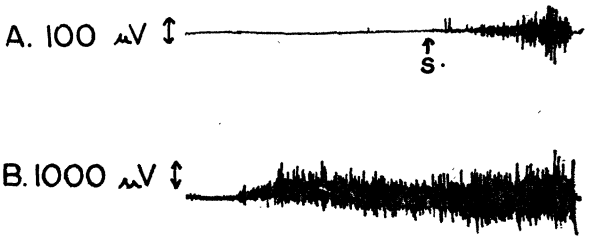

FIG. 1. Effect of contraction of the biceps on the simultaneous contraction of the triceps. The elbow is extended against maximal resistance; surface electrodes on the triceps account for tracing *B*. During this extension, at point *S*, the forearm is supinated while a recording from the biceps is made to give tracing *A*. An Offner Electromyograph with pen recorder was employed. Results indicate that during volitional extension of the elbow, the intensity of contraction of the triceps is not decreased by simultaneous supination of the forearm in which the antagonistic biceps plays a major role. The voltage gain has been adjusted so that voltages below 20 μv are not recorded.

onist begins to respond in cocontraction. The contraction of the agonist is far greater in degree than that of the antagonist, but cocontraction does occur.

As a matter of fact, the biceps and triceps will only act as antagonists if flexion or extension of the elbow is the only movement involved. If, on the other hand, the forearm is supinated during extension, full cocontraction between the biceps and the triceps occurs routinely. Furthermore, if the forearm is supinated, there is no appreciable inhibition of potential observed in the triceps when maximum resistance is applied to extension of the elbow (Fig. 1).

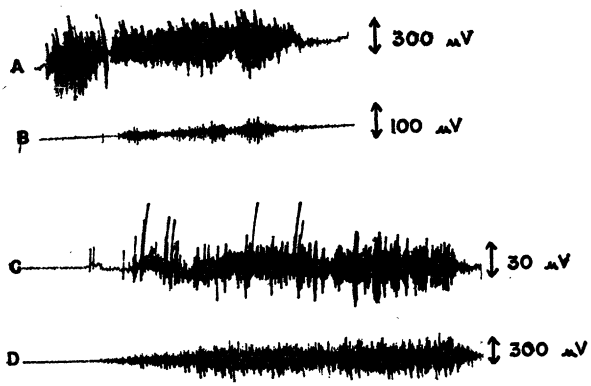

FIG. 2. Cocontraction of the antagonist muscles at the ankle during unimpeded plantar-flexion and dorsiflexion. *A*, potential obtained from the lateral head of the gastrocnemius during plantar-flexion beginning in the neutral position for the ankle; *B*, potential obtained from the anterior tibial muscle simultaneous with that recorded in *A*; *C*, potential obtained from the lateral head of the gastrocnemius during dorsiflexion of the ankle beginning in neutral position; *D*, potential obtained from the anterior tibial muscle simultaneous with that in *C*. Potential is recorded in tracing *B* simultaneously with the onset of contraction in *A*, but because of voltage gain setting, the initial low voltages in *B* are not evident in the tracing.

One type of cocontraction which has been generally neglected is the type which occurs in all antagonistic muscles in the shortened range of agonist contraction. As the agonist goes into the final range of contraction, it begins to cause proprioceptive stimulation through stretch reflexes of the antagonist muscles. The resulting contraction of the antagonist then offers resistance to the final phase of movement of the agonist, so that we have in the final movement phase of contraction a dynamic interrelationship between the contraction of the agonist and the antagonist. At the point at which the antagonist begins to contract, as a result of the proprioceptive stimulation, the agonist shows an increase in response as a result of the opposing pull of the antagonist. Quantitatively, the angle at which this phenomenon presents itself will vary with the joint and the muscles involved. In the biceps this occurs at an angle of flexion greater than 90° (the exact angle will vary with the individual), whereas at the ankle (Fig. 2) it begins to occur almost immediately and builds up to a maximum at a point in the range of flexion corresponding to the limit of the range of passive motion. The explanation for the variation between the ankle and the elbow lies in the fact that, in the elbow, the passive range of motion is very much greater than it is in the ankle. In the ankle any motion at all begins almost immediately to involve the antagonist, so that cocontraction becomes the rule in practically all motions involving the ankle.

Whereas it has been difficult to demonstrate reciprocal innervation in voluntary movement, one would expect that such would not be the case in reflex activity. Sherrington utilized the knee jerk for this demonstration. There is one condition under which we have been able uniformly to demonstrate reciprocal innervation in the human, and that is in spasticity. Many patients with neuromuscular disease evidence exaggerated activity of the spinal stretch reflex which manifests itself clinically as an increased tendency toward muscle contraction, especially during passive manipulation. This is defined as spasticity, and eventually this condition, if uncorrected, leads to contracture, a structural shortening of the muscles involved. Spasticity interferes with the full utilization of any voluntary power which the muscles may retain after paralysis and also limits the range of motion possible through movement of the joint. It thus becomes an important problem in the rehabilitation of patients with neuromuscular disease. Our own thinking has compared some forms of spasticity to decerebrate rigidity as first described by Sherrington. In this we concur with the hypothesis of Magoun and his co-workers (*5*). It was on the basis of this reasoning that we felt that reciprocal innervation should apply to spasticity in the same way that Sherrington was able to demonstrate so clearly for decerebrate rigidity. We, therefore, stimulated electrically muscles antagonistic to those exhibiting spasticity and found that relaxation of the spastic muscles could be demonstrated easily. Faradic current applied to the motor point with sufficient intensity to give a maximum contraction of the antagonist was employed. The current was applied for periods of 1 min or longer. Relaxation at times occurred instantly and at other times occurred after a short delay. Sherrington used electrical excitation of motor nerves (*1*) in animals to obtain this same form of relaxation in the demonstration of reciprocal innervation.

The relaxation was utilized to bring the affected limb through its whole range of motion. As a result, not only was relaxation evident during the application of electrical stimulation, but a persistence of the relaxation was evident in some cases for days following stimulation. With the release of the affected muscle from spasticity, techniques of neuromuscular re-education described previously (*6*) were employed to facilitate the development of latent power to its maximum. Such muscle power, which would permit the patient to carry the limb or the affected part through the full range of motion, would minimize the possibilities of a further increase in spasticity. Spasticity could also be relieved in varying degrees in those paralyzed patients where residual muscle power was not sufficiently great to bring about the restoration of voluntary movement. In such cases relaxation

of the spasticity through electrical stimulation of the antagonists permitted the passive movement of the limb through a greater range and in this way helped minimize the recurrence of the spasticity, thereby cutting down the possibilities of contracture. Details of the procedure will be described elsewhere (*7*).

We may summarize our observation by stating that in normal voluntary movement in man there is at present insufficient evidence that reciproeal innervation plays the role in the coordination of the contraction of antagonist muscles which is assumed for it by most thinking on kinesiology. Cocontraction seems to be the rule rather than the exception. On the other hand, we were able to demonstrate reciprocal innervation in patients with neuromuscular disease who showed evidence of spasticity.

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Systematic Status of the Pure Culture Ciliate known as *"Tetrahymena geleii"* and *"Glaucoma piriformis"*

John O. Corliss[1]

Laboratoire d'Embryogénie Comparée, Collège de France, Paris

Since Lwoff's (*1*) success in establishing a small holotrichous ciliate in axenic culture (i.e., free from other microorganisms), at least 50 identical or closely related members of the *Colpidium-Glaucoma-Leucophrys-Tetrahymena* group have been so grown. Some 30 of these organisms are still being maintained in various laboratories and have been used in over 250 investigations, principally of a physiological or biochemical nature, within the past 15 years (*2, 3*). The increasing importance of the experimental animals has made highly advisable a comparative morphological study in order to establish their probable taxonomical interrelationships. Twenty-six of the pure culture strains have been investigated, employing, in particular, the method of silver impregnation, an invaluable technique in study of such small and relatively undifferentiated ciliates. The present report is concerned chiefly with the 21 strains which I consider to be members of a single species but which, to date, have been carried in the literature under several different names, the most common two in recent years being *Tetrahymena geleii* Furgason, 1940, in America and *Glaucoma piriformis*[2] (Ehrenberg, 1830) Maupas, 1883, in Europe.[3] The history of these strains has been traced (*2*).

All the strains studied fall within the limits of the following brief characterization of this very widely distributed species:

Body typically pyriform in shape, 26–92 μ in length, average size about 50 μ × 30 μ; 17–22 ciliary meridians, usually 19–20, consisting of well-defined primary and secondary portions; generally 2 postoral kineties, unipolar meridians with anterior ends terminating directly at posterior margin of cytostome. Delicate apical loop at morphological apex of body; preoral suture single or double fibril from loop to cytostome; 3 intermeridional connectives, anterior end of body, roughly concentric about apical loop. Cytostome pyriform, 9–11 μ in length, about 5 μ from anterior end of body, oriented directly in body axis; characteristic tetrahymenal buccal ciliature consisting of right-hand undulating membrane and left-hand adoral zone of 3 membranelles, bases of the latter oriented at an angle of about 45° to axis of cytostome. Two to three permanent contractile vacuole pores, diameter 1 μ or less, typically located near posterior end of body in meridians 5 and 6; cytoproct slitlike in posterior end of stomatogenetic meridian 1. Macronucleus ovoid to irregularly spherical, generally not greater than 11 μ in any diameter, centrally located or slightly posterior, exhibiting typical chromatin extrusion during fission; micronucleus often absent (see below). Conjugation never observed; cysts reported by one worker (*4*).

In a study of the micronuclear problem presented by this species I have employed the Feulgen technique in critical observation of ciliates, both from axenic strains and from a number of more recently isolated bacterized strains. To date, I have examined 13 pure culture strains, using organisms from 18–20-hr cultures (rich in dividing forms) and 5–7-day cultures, and I have found all of them to be amicronucleate. The axenic strains in question were originally isolated in France, England, and in four widely separated geographical areas in the United States. Three of the American strains had been reported to be amicronucleate (*5*). Five strains, more recently isolated from various localities around Paris, and grown only in bacterized cultures, are also without micronucleus. In addition, in more than 6 cases in which the species has been found as a facultative parasite in the body cavity of living chironomid larvae (*Chironomus plumosus*), it is entirely amicronucleate.[4] A coprophilic

[1] Atomic Energy Commission postdoctoral research fellow in the biological sciences, Oct. 1951–Oct. 1952.

[2] The trivial name was originally spelled "pyriformis" but has been written with an "i," in particular by French protozoologists, for the past 30 years.

[3] Very recently the French investigators Fauré-Fremiet and Lwoff, in several separate publications (cited by Corliss [*2*]; most recent being Lwoff's footnote, p. 325, in Kidder and Dewey [*3*]), have employed the name *Leucophrys piriformis* in reference to a number of the strains. Both these workers are now in agreement with the writer that the species should be called *Tetrahymena pyriformis* (personal communications).

[4] I have also isolated a second, very closely related, species of *Tetrahymena* from *Chironomus*, sometimes from the same larvae. It is frequently found in conjugation and is very likely the ciliate reported once before (*6*). Its micronucleus is prominent, generally 2.5–3.0 μ in diameter. Full description will be published later.