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CHISHOLM'S SECOND LAW OF HUMAN INTERACTION:

When things are going well, something will go wrong.

Corollary I: *When things can't get any worse, they will.*

Corollary II: *Any time things appear to be going better, you have overlooked something.*

CHISHOLM'S THIRD LAW OF HUMAN INTERACTION:

Purposes, as understood by the purposee, will be judged otherwise by others.

Corollary I: *If you explain something so clearly that nobody can misunderstand, somebody will.**

Corollary II. *If you do something which you are sure will meet with everybody's approval, somebody won't like it.*

Corollary III. *Procedures devised to implement the purpose won't quite work.*

Lest the unwary dismiss these principles as ephemera and of no real application, it is stated in the strongest possible terms that the very simplicity of these laws conceals the mainspring of human destiny. Like Graham's Pronouncement, *You can only spend it once* (which conveys in a single brilliant sentence all that needs to be known about personal and national "budgetry"), these important laws make clear to the discerning eye the reasons for human frustration, mishap and delay.

Chisholm notes that "a number of mostly pseudonymous investigators", in various engineering and laboratory contexts, have identified new elements such as the Finagle factor and Diddle's constant during the investigation of frustration phenomena. For example, it has been observed that no matter how carefully an experiment is planned, something *always* goes wrong, usually in precisely the operation which *could not* go wrong. The difference between expected and achieved results can be expressed in an exact relation, called the Snafu equation, which employs the Finagle constants. An organization, the International Society of Philosophic Engineers, has recently published observations such as the following: *In any calculation, any error which can creep in will do so;* and *Any device requiring service or adjustment will be least accessible.*

As the application of Newton's laws of motion laid the foundation for the physical sciences, so the elucidation, application and exploitation of these laws of human interaction should, at one tremendous stroke, elevate human life to an exalted and Olympian plane.

The Editors wish to thank Dr. Frank I. Jackson of Regina for drawing Professor Chisholm's work to their attention.

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*This concept was propounded independently in 1595 by Shakespeare's publisher, Ambrose De Vere Cullhoope, of Botched Galley, Surrey, who called it "The Axiom of Editorial Anguish".

SUBARACHNOID DISTRIBUTION OF DRUGS AFTER LUMBAR INJECTION

IN diseases that diffusely involve the meninges systemic therapy is preferable if the drug is freely able to penetrate the blood-CSF (cerebrospinal fluid) barrier. High levels of a drug may then be maintained in spinal fluid by continuous systemic administration, and the drug reaches all surfaces bathed by the spinal fluid. On occasion, the pathologic process may so alter the barrier that drugs that are normally excluded do enter the spinal fluid. However, in the case of meningeal leukemia, infiltration of the meninges by leukemic cells does not alter the virtual exclusion of the systemically effective antimetabolites from the spinal fluid. Therefore, intrathecal administration is essential in such an instance. This imposes a potential limitation on therapeutic efficacy, since successful treatment depends upon distribution of the drug throughout the entire subarachnoid space after injection into the lumbar sac.

By means of autoradiography and contrast radiography in monkeys and by three-dimensional external scanning, autoradiography and histologic observation in human patients, Rieselbach *et al.* (*New Engl. J. Med.*, 267: 1273, 1962) have attempted to determine the subarachnoid distribution of material injected into the lumbar sac. I^{131}-rose bengal was injected into the lumbar sac of 12 *Macaca mulatta monkeys.* The drug was instilled in volumes so as to comprise 0.7% to 42% of estimated spinal fluid volume. X-ray films of the entire subarachnoid space were taken after injection to indicate distribution of dye. A lethal dose of pentobarbital was administered and the monkeys were rapidly frozen; sections of the frozen head were prepared for autoradiography.

Radioactive colloidal gold (Au^{198}) was injected into the lumbar sac of one monkey (with subsequent autoradiography) and eight patients. Six of these patients had meningeal leukemia and two had medulloblastomas. Au^{198} was injected in volumes ranging from 11% to 33% of estimated cerebrospinal fluid volume. Subsequently, external scintillation scanning was performed.

The results demonstrated that the volume of injected solution is an important factor in attaining widespread distribution of drugs instilled in the lumbar sac. With a volume approximately 10% of estimated CSF volume, significant concentration was achieved in the basal cisterns of the monkeys; with a volume approximately 25%, distribution was obtained throughout the cerebral subarachnoid space and ventricular system. In the patients, external scanning confirmed the observations in monkeys, that lumbar instillation in volumes greater than 10% of estimated CSF results in significant drug concentration reaching the basal cisterns. The most diffuse distribution of radioactivity was obtained in the patients receiving the greatest percentage of estimated CSF.