sula of Quebec, Canada, have shown that the citrate-soluble metal content of stream alluvium is a useful method of appraising the possibilities of mineral deposits in the area upstream from the sample site. Samples of alluvium may be taken either from the active bed of the stream or from terrace deposits. Field trials showed the presence of trains of alluvial material containing a higher-than-normal quantity of extractable metal for distances up to 4 mi, and in one case for 50 mi downstream from the deposits. The content of extractable metal depends to a certain degree on the grain size, organic content, and mineral composition of the sample as well as on the distance from the source.

On the basis of these experiments and subsequent experience, regional surveys of the citrate-soluble heavy-metal content of stream alluvium is recommended as a reconnaissance method of mineral exploration.

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1. H. Bloom. *Additional Field Methods Used in Geochemical Prospecting* (Released by U.S. Geological Survey as open-file report, 16 Sept. 1953, pp. 28–31; *Econ. Geol.*, in press.

21 April 1955

Statistics

As a nonstatistician user of statistical methods, I feel moved to reply to the communication from Frederick Sargent, II, [*Science* **121,** 402 (18 Mar. 1955)]. There is a danger, in my opinion, that the very real case against indiscriminate use of correlation analysis may be stultified by the continued citation of nonsense correlations to support it. That noncausal correlations do exist has already been adequately demonstrated. Offhand I can think of the correlation between birth rate and marriages in the Church of England, and that between stage of the Potomac River and street traffic flow in Washington, D.C., adduced respectively, I believe, by Pearson and Ezekiel.

Actually, the correlations found are but formalizations of common-sense statements: "The summer months, when both precipitation and temperature are high (in Chicago) have shorter names than the others" (the "r" months have provided centuries of oyster eaters with a handy mnemonic); "Both birth rates and church marriages have declined in England"; "Street traffic and river flow have similar diurnal variations."

It would be more useful to students to point out forcibly the need for *a priori* biological hypotheses for correlations to be tested than to produce further examples of noncausal correlations, no matter how amusing.

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Steroid Anesthetic Agent

Since Selye (*1*) and others reported the central depressant action of certain steroidal hormones, little attention has been given to the quantitative and qualitative comparison of the anesthetic action of steroids and the commonly used anesthetics. The possible use of this type of compound in clinical anesthesia led us to study the relationship of chemical structure to activity in a series of steroids. 21-Hydroxypregnane-3,20-dione sodium succinate (hydroxydione) (*2*) was found to be the most promising of a number of water-soluble steroids. The marked anesthetic action, solubility in water, and lack of endocrine activity and other side effects have justified the evaluation of this compound in man as an intravenous anesthetic (*3, 4*).

On intravenous injection, anesthesia is produced by hydroxydione in mice, rats, cats, dogs, and monkeys (*5*). In the mouse and rat the most striking features of hydroxydione are its remarkably high anesthetic potency, which equals that of Pentothal Sodium (thiopental sodium), and its therapeutic index, which greatly exceeds that of the thiobarbiturate (see Table 1). However, in cats, dogs, and monkeys, hydroxydione is not as active (milligram for milligram) as thiopental sodium is. In dogs, hydroxydione at 100 mg/kg compares in effectiveness with 25 mg of thiopental sodium. However, hydroxydione is much less toxic than thiopental sodium—three of seven dogs died after intravenous injection of 50 mg of thiopental sodium per kilogram of body weight, but only one of eight dogs died after intravenous injection of 300 mg/kg of hydroxydione.

Table 1. Comparative intravenous anesthetic potencies of thiopental sodium and hydroxydione in mice

Compound	AD_{50} (mg/kg)	LD_{50} (mg/kg)	TI (LD_{50}/AD_{50})
21-Hydroxypregnanedione sodium succinate (hydroxydione)	21.5	250	11.5
Thiopental sodium	19.5	80	4

Other advantages of the anesthesia produced are the relatively low degree of respiratory depression and rapid uncomplicated recovery with minimum postanesthetic depression. Little or no endocrine activity can be demonstrated after administration of large doses of hydroxydione to experimental animals (*6*).

In view of the striking pharmacological effects of hydroxydione, it is of interest to reconsider the possible actions of endogenous hormones and their metabolites on the central nervous system, such as in central control of anterior pituitary secretion, where certain analgesics and hypnotics have been shown to exert marked effects. Other central actions of hydroxydione, such as effects on brain metabolism (*7*) and electroshock threshold (*8*), as well as effects in combination with other drugs, are being investigated and will be reported subsequently.

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References and Notes

1. H. Selye, *Endocrinology* 30, 437 (1942).
2. 21-Hydroxypregnanedione acid succinate wat prepared by a synthesis involving the catalytic hydrogenation of desoxycorticosterone followed by succinoylation, mp 195°–197°C; $/a/_D + 95°$ ($CHCl_3$); $\lambda\lambda_{max}^{KBr}$ 5.70, 5.87, 7.01, 7.21, 7.36, 7.68, 8.60, 8.99; M.W. 432; the sodium salt was prepared as a white free-flowing lyophilate, readily soluble in water or mildly alkaline buffer solutions. Viadril[R] brand of hydroxydione is the registered trademark of Chas. Pfizer and Co., Inc., for hydroxydione, 21-hydroxypregnane-3,20-dione sodium succinate.
3. G. S. Gordan *et al.* have studied hydroxydione in a number of patients and have found this agent to be a safe, convenient, and practical basal anesthetic for surgical procedures in man. Report is in preparation.
4. During the course of our clinical studies, a report appeared in which sleep was induced in man by intravenous administration of progesterone [W. Merryman *et al., J. Clin. Endocrinol. and Metabolism* 14, 1567 (1954)].
5. S. Y. P'an *et al.*, in preparation.
6. J. F. Gardocki and S. Y. P'an, in preparation.
7. G. S. Gordan and H. W. Elliott, *Endocrinology* 41, 517 (1947).
8. D. M. Woodbury, *J. Pharmacol. Exptl. Therap.* 105, 27 (1952).

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