History does not repeat itself in every detail but it does move in cycles. The use of digitalis in the witch doctor's brew was intuitive and empirical. Withering made its use respectable. However, he continued to use it indiscriminately for dropsy whether due to heart failure or kidney failure. Sir James Mackenzie, that master of general practice as well as of English prose, put the use of the drug on a scientific basis early in this century. He showed that digitalis will relieve the heart failure of a patient with rapid auricular fibrillation. It delays conduction through the bundle of His and slows the rate of the ventricle. Thus that chamber has time to fill before it pumps out the blood during each contraction.

Anybody who has perfused the heart of an animal knows that the cardiac glucosides when given in toxic doses cause the ventricle to contract more forcibly for a little while. However, if the dose is sufficient to stimulate, the initial stimulation is in all cases followed by spastic paralysis of the heart muscle. This toxic effect occurs sooner in the damaged heart than in the healthy heart.

The "modern" advocates of digitalis for all kinds of heart failure seem to have learned from the pharmacologists about its initial stimulating action only. How many people have died because doctors who did not study medical history and who lacked a broad knowledge of medicine did not know the toxic properties of digitalis on the heart ?

History should not depress us. Rather should we study it so that we can avoid past mistakes and escape blame by the future. When all doctors rode horses they knew that you can make the lame or tired animal go faster for a little while if you beat him. However, if you abuse the poor dumb animal in this fashion he will fall going over the next jump or even drop dead before reaching it.—I am, etc.,

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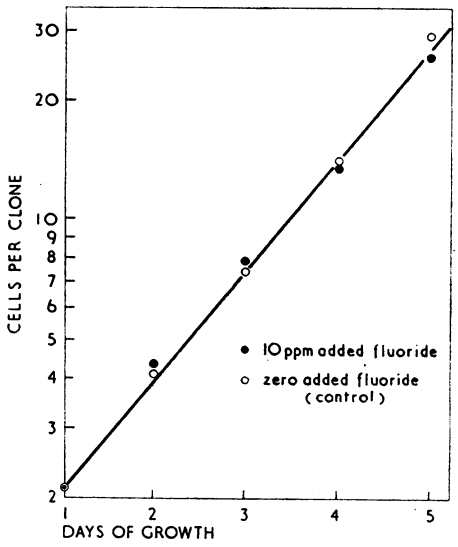
Sodium Fluoride and Cell Growth

SIR,—Armstrong and colleagues (20 February, p. 486) found that *circa* 15 p.p.m. fluoride is required to inhibit growth of human epithelial cells *in vitro*, whereas Berry and Trillwood[1] had previously indicated that as little as 0.045 p.p.m. fluoride reduced the multiplication of HeLa cells in culture. Dr. Berry and Mr. Trillwood entered a rejoinder (20 March, p. 793) that our cells did not multiply at a rate sufficient to allow the inhibitory effect of fluoride to be revealed. While not acceding to the validity of this criticism of our work, we now present the results of experiments which should satisfy the objections to our first study, and we report new findings confirming the low order of effect of fluoride on HeLa-cell growth.

The culture medium was that previously used. HeLa cells from a 4-day monolayer were dispersed by trypsin and diluted in growth medium to give two cell suspensions of known cell count. Replicate flasks (30 ml., Falcon Plastics) at each fluoride concentration (0.0, 1, 5, and 10 p.p.m. added fluoride) were prepared to contain 4.5 ml. medium and 0.5 ml. cell suspension (108 cells in one series and 215 cells in a second series). The *p*H of the media was maintained at 7.3 during incubation by an atmosphere of 2.5% CO_2. The flasks were examined microscopically after 24 hours of incubation and the positions of 5 cells in each flask which had divided once were marked. The number of cells in each of these clones was recorded at 24-hour intervals but clones which had not divided into 4 cells on day 2 were abandoned. Cell counts were discontinued after the fifth day when the cells were too numerous for accurate enumeration. All counts of cell population and number of clones were made by one of us (M. E. P.) without knowledge of the fluoride contents of the media, which did not change during an 11-day period.

Each point in the Graph gives the average cell count of 36 to 54 clones and these counts were not affected by the size of the inoculum. The results obtained with media containing 1 and 5 p.p.m. fluoride were also indistinguishable from those of the controls. The generation times of the cells in the four media were : 0 F—1.1 days ; 1 p.p.m. F—1.1 days ; 5 p.p.m. F—1.1 days and 10 p.p.m. F—1.2 days, and are to be compared with a doubling time of about 30 hours obtained by Dr. Berry and Mr. Trillwood (20 March, p. 793) with media not containing added fluoride. We regard these results as confirmation of those of our previous study (20 February, p. 486) and to be a further demonstration that much higher concentrations of fluoride than those reported by Berry and Trillwood (0.045 to 4.5 p.p.m.) are required to reduce the growth of HeLa cells in culture.



Dr. Berry and Mr. Trillwood now suggest (20 March, p. 793) that attachment of HeLa cells to a glass surface may be the step at which the cells are most sensitive to the action of fluoride. This suggestion is made even though they originally reported that 4.5 p.p.m. fluoride did not reduce the number of clones formed on *plastic* surfaces, while finding that 0.045 p.p.m. fluoride reduced the number of cells. In the present experiments the mean number of clones in the flasks which had contained media of 1 and 5 p.p.m. fluoride equalled or exceeded the mean clone count of the control flasks with the same size of inocula. However, the mean number of clones formed from media with 10 p.p.m. fluoride were 84% and 79% of the control clone count for the larger and smaller inocula, respectively. Thus, there is a possibility that concentrations of fluoride of the order of 30 to 50 times that of human body fluids may affect HeLa cells, *or the vessel surface,* to impede attachment of cells to glass or plastic surfaces. Nevertheless, alteration of HeLa-cell multiplication by fluoride, which is the feature of biologic significance and that originally claimed by Berry and Trillwood as an effect of fluoride, requires, according to the results of our two studies, a concentration of fluoride greatly in excess of that given in the original report of the Oxford workers.

Dr. Berry and Mr. Trillwood now indicate that they have never interpreted their results in respect to the safety or hazard of public water fluoridation. This clearly stated disclaimer will do much to counteract the unintended but unfortunate implications of some statements in their original report.—We are, etc.,

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REFERENCE
1 Berry, R. J., and Trillwood, W., *Brit. med. J.*, 1963, 2, 1064.

Department for Venereal and Sexually Transmitted Diseases

SIR,—For many years I have been anxious about the narrowness of the classification of the nomenclature of diseases treated at so-called "Venereal Disease Clinics." These were, of course, formed following the passing of the Venereal Diseases Act of 1916. I welcome therefore most heartily the new Department for Venereal and Sexually Transmitted Diseases at the Middlesex Hospital (15 May, p. 1305).

It is known that experienced workers have in many cases ignored the "official" position and have diagnosed and treated these diseases at such clinics, merely including such infections under the large group of "other infections." This camouflage is not good enough and I am delighted that the necessity for a new approach has been more widely recognized.

It was for this reason that when the London Lock Hospital was the principal hospital for this type of infection its consultants had each to be on the staff of another hospital as either a genito-urinary surgeon, a dermatologist, a general surgeon, or a gynaecologist, and possessed of a higher qualification, either the F.R.C.S. or the M.R.C.P.

It is to be hoped that this far-seeing action of the Middlesex Hospital will be followed by others.—I am, etc.,

London W.1. GLADYS M. SANDES.

C.S.F. Protein in Multiple Sclerosis

SIR,—Professor Henry Miller, in making an unfortunate mistake in an otherwise good review of an excellent book (27 March, p. 847) on multiple sclerosis by Drs. McAlpine, Lumsden, and Acheson,[1] may have misled some clinicians. He has stated that a simple colorimetric method for measuring spinal fluid gamma-globulin "represents" a real diagnostic advance and that such a method is in routine use at a teaching hospital not a hundred miles from Leeds. This is, indeed, surprising, because no simple colorimetric method for the estimation of gamma-globulin has yet been devised.