Fig. 1 shows also that heating the purified virus preparation for different periods at 53° C progressively reduces the capacity of the virus to cause a decrease in viscosity. These results with heated virus have a correlate in the reduction of the inhibitor destroying capacity of virus consequent to heating (*7*).

Studies of the effect of convalescent antiswine influenza swine serum showed that a quantity of serum capable of neutralizing completely the hemagglutinative activity of the virus prevented completely the typical effect of virus on inhibitor viscosity. The same amount of normal swine serum was somewhat less effective. The dependence of the rate of viscosity reduction on virus concentration and on the state of the virus, i.e., whether the virus was heated or not heated, as well as the absence of viscosity changes in the presence of immune serum, suggests that the reduction in viscosity is related to an interaction of the virus particles themselves with the viscous component of inhibitor solutions.

There are several reasons for supposing that the relationship of the EW inhibitor of hemagglutination to the viscous component of solutions of purified inhibitor is one of identity: (a) both the inhibitor and the viscous component appear capable of interacting with virus; (b) both suffer a change when treated with unheated virus, and both are less susceptible to action by heated virus; (c) the viscous component has probably a high molecular weight, and it is likely that any material of high molecular weight which is capable of combining with virus would be capable also of inhibiting virus hemagglutination; and (d) the specific viscosity of the two purified inhibitor preparations, A178 PIII EI and A180 PEI, which have been studied in detail, is proportional to the inhibitory activity. Calculated on a nitrogen basis, the activities of these preparations were 41 and 60 times, respectively, that of EW, and the specific viscosities at 30 γ N per ml were 0.075 and 0.105. This proportionality becomes a valid test when it is considered that the viscosity of purified inhibitor solutions is contributed chiefly by a component (or components) which is susceptible to virus action, as inferred from the low terminal viscosities of virus inhibitor mixtures.

The reduction in viscosity induced by virus may be interpreted as a reduction in the asymmetry of the molecules (or particles) susceptible to virus action. There are several obvious and quite different ways by which such a change in shape could be achieved: (a) the molecules could be fragmented across the long axis; (b) they could be made to fold or coil without change in size; (c) they could be made to condense with one another with simultaneous increase in size and decrease in asymmetry; and (d) they could form suitable stable complexes with virus particles. Of these ways, the first three could be thought to depend on an enzymatic action of the virus, while the fourth could be regarded as a process of stable aggregation of inhibitor molecules and virus particles. Support for the latter explanation is provided by the observation (*6*) that a precipitate forms at interfaces between EW and purified virus preparations. No definite evidence of precipitation has been obtained, however, in the present experiments with dilute solutions of purified inhibitor; and since inhibitor virus mixtures which have been incubated for long periods possess considerable hemagglutinative activity, comparable to that of uninhibited virus, it is likely that the virus separates from the viscous component after interaction. Accordingly, an enzymatic hypothesis of virus function offers the most reasonable explanation at the present time of the virus induced reduction in viscosity of solutions of purified inhibitor. This hypothesis is compatible also with the relative independence of the terminal viscosity on initial virus concentration and with the failure of repeated additions of fresh inhibitor solution to affect appreciably the viscosity reducing capacity of virus.

If the above interpretation is correct, the present observations provide the most direct demonstration, so far as we are aware, of an enzymatic action of influenza virus on a relatively pure and simple substrate. It should be mentioned that several previous attempts (*1, 2*) at such a direct demonstration have failed.[3]

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A New Human Hereditary Blood Property (Cellano) Present in 99.8% of all Bloods

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A new agglutinogen of human blood was recently observed with the aid of an immune agglutinin produced by a mother of an infant with a mild form of hemolytic disease.[1] This antibody, which behaves like a "warm" agglutinin (*4*), is remarkable because of the unusually

[1] The diagnosis was made by Dr. Eric Ponder on the basis of clinical and hematologic studies.

[3] While this paper was in press, D. W. Wooley (*J. exp. Med.*, 1949, **89**, 11) reported changes in the viscosity of erythrocyte extracts on treatment with influenza virus A (PR8 strain).

high incidence of positive reactions (99.8%) in tests of 2500 blood specimens submitted for Rh testing. When first studied in May 1947, its titer at 37° C, in saline, was 1:64 and 18 months later its activity was only slightly diminished (1:32). Its titer was 1:1 at 20° C and 1:4 at 5° C. Absorption experiments with numerous blood specimens of different antigenic structure indicate that the high incidence of positive reactions is attributable to the action of a single antibody.

For want of a better name, this blood factor will be referred to by the patient's name, "Cellano", and its antibody as "anti-Cellano."

Of the 2500 blood specimens tested with anti-Cellano, more than 90% were from women whose Rh negative blood was submitted for antibody determination. Excluding the blood of the immunized mother, only five were found to lack the Cellano factor (0.2%). The antigenic structure in these five and in the patient's blood is given below:

		Reactions with Anti-					
		D	C	E	c		
1.	Patient Cellano	A	N	+	+ o +	Rh pos.	(Rh_1)
2.	Mrs. B. M.	O	MN	o	o o +	Rh neg.	
3.	Mrs. B. H.	A	M	o	o o +	Rh neg.	
4.	Mrs. R. C.	A	MN	o	o o +	Rh neg.	
5.	Mrs. L.	O	MN	o	o o +	Rh neg.	
6.	Julian K.	B	M	+	+ o +	Rh pos.	(Rh_1)

The findings in the family of Julian K., whose blood lacks the factor, follow:

	Reactions with Anti-					
	D	C	E	c		Cellano
Father:						
John K., Sr.	O	MN	+	+ + +	Rh pos. (Rh_1Rh_2)	+
Mother:						
Mary K.	AB	M	o	o o +	Rh neg.	+
Children:						
1. John	A	MN	+	o + +	Rh pos. (Rh_2)	+
2. Julian	B	M	+	+ o +	Rh pos. (Rh_1)	o
3. Mrs. I. S.	A	M	+	+ o +	Rh pos. (Rh_1)	+
4. Mrs. A. G.	A	M	+	+ o +	Rh pos. (Rh_1)	+
5. Mrs. A. V.	A	M	+	+ o +	Rh pos. (Rh_1)	o
6. Frank	B	M	+	+ o +	Rh pos. (Rh_1)	o
7. Andrew	A	MN	+	+ o +	Rh pos. (Rh_1)	+
8. Josephine	A	MN	+	+ o +	Rh pos. (Rh_1)	+

Apparently, both parents are heterozygous for the factor so that 25% of the offspring are expected to be Cellano negative. Of the eight children tested, three were found to lack this new property.[2]

Assuming the presence of two genes at a particular locus on one of the chromosomes, their incidence could be calculated as follows:

Let Y = gene determining the presence of the Cellano factor and y = gene determining the absence of the Cellano factor

[2] For these specimens the authors are indebted to Mr. Benson Rosenberg, Elizabeth Biochemical Laboratory, Elizabeth, New Jersey, who also tested 350 random blood specimens, all of which contained the Cellano factor.

Then (1) $Y + y = 1$

(2) $y = \sqrt{\text{Cellano negative}} = \sqrt{.002} = .045 = 4.5\%$

(3) $Y = 1 - .045 = 0.955 = 95.5\%$

(4) $Y^2 + 2Yy + y^2 = 1$

(5) $(.955)^2 + 2(.955)\ (.045) + (.045)^2 = 1$

(6) Cellano homozygous = .912 or 91.2%
Cellano heterozygous = .086 or 8.6%
Cellano negative = .002 or 0.2%

Blood lacking the factor can be expected only in the offspring of the following matings:

$Yy \times Yy = 8.6 \times 8.6 = 0.74\%$ of all matings (1:135)
$2Yy \times yy = 2(8.6)(0.2) = 0.03\%$ of all matings (1:3333)
$yy \times yy = (0.2)(0.2) = 0.0004\%$ of all matings (1:250,000)

In the remaining matings (99.23%), all the offspring must be Cellano positive.

In a series of 150 Negroes, all blood specimens were found to contain the Cellano factor.

In the white population of the United States, the Cellano factor has a greater incidence than any other factor, exceeding the factor e (h″) by 2.8% (*7*). In this connection, it may be noted that in American Indians (*3*), and Chinese (*6*), the D factor (Rh_0) has an incidence of 99% or higher, and certain races of American Indians are almost exclusively of group O.

Correlated studies indicate that the Cellano factor is independent of the AB, MN, and Rh-Hr systems. This view was confirmed in a study of the Cellano serum made available to Dr. R. R. Race and his colleagues (*8*).

A list of Cellano negative blood is being prepared for the purpose of identification of other antibodies which are characterized by a high incidence of positive reactions. Such blood would be essential for transfusing those rare patients who may have produced this antibody and also for transfusing their affected infants.

The genetic homologue of the Cellano factor, when found, would be a blood property present in 8.8% of the same population of which 0.2% would be homozygous and 8.6% heterozygous. Two human antibodies have been described which do give a frequency of positive reactions closely approximating this value (anti-Lutheran 8% and anti-Kell 7%) (*2, 1*).

Parallel tests on the above-mentioned family with the anti-Cellano serum and two specimens of anti-Kell serum, one of which was supplied by Dr. R. R. Race, show that the genes for Cellano and Kell antigens are alleles (*5*). The findings indicate that both parents are heterozygous for Kell as well as for Cellano. This would lead to an expectation among their offspring of ¾ Kell positive and ¼ Kell negative. In exact agreement with this, and in striking contrast to the frequency of 8.8% calculated to exist in the entire population, six of the eight children were Kell positive.

For the sake of uniformity, the letters "*K*" and "*k*," already used by the British workers for the genes determining Kell positive and Kell negative reactions respectively, will be retained (*9*). The observations with anti-Cellano indicate that the gene *k* can now be considered as indicating the presence of the Cellano factor. As in the case of *M* and *N* and the three Rh-Hr systems,

there are three genotypes (*KK, Kk, kk*) corresponding to three phenotypes.

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A New Time Scale for Kymograph Recording

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In laboratory experiments involving the kymograph recording of biological responses a time line is generally traced on the smoked paper, together with the experimental record. This time line allows the observer to correlate the observed phenomenon with absolute time.

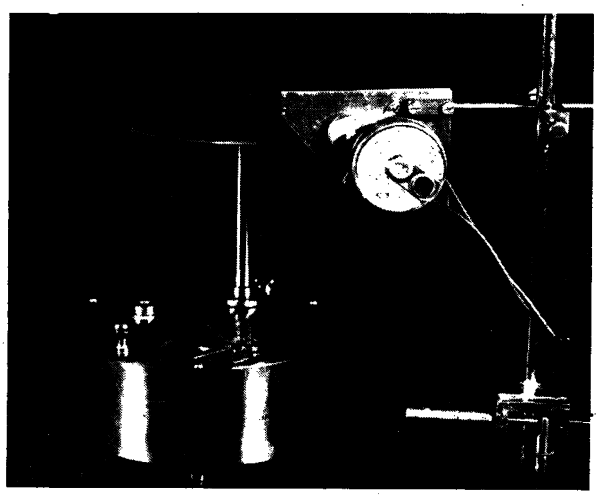

FIG. 1. The new interval timer for kymograph recording, in use.

With the usual equipment available in the laboratory, tracing this time line involves the use of signal magnets, dry cells, and a signal source. Failure on the part of any of these units leads to inconveniences. When the signal source is centrally located and is used by several investigators in different experiments, the adjustment of the signal may not be suitable for all. To overcome these troubles, a small instrument which is independent of such auxiliary apparatus has recently been developed. This instrument is a small self-contained unit (Fig. 1) which will trace a characteristic time scale when plugged into any 110-volt, 60-cycle circuit. Although the intervals on this scale are not adjustable, the form of the time scale traced makes it suitable for use over a wide range of kymograph speeds. (See Fig. 2.)

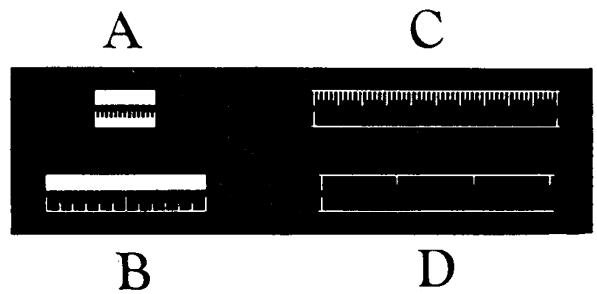

FIG. 2. Four examples of the new time scale for kymograph recording, illustrating its enormous range. The upper base line indicates intervals of 1 sec (long lines) and ⅕ sec (short lines). The lower base line similarly indicates 1-min and 10-sec intervals. Note that, at very slow drum speeds, the 1-sec and ⅕-sec divisions merge into a solid phalanx. (A) At drum speed of 0.5 mm/min. (B) At drum speed of 10 mm/min. (C) At drum speed of 200 mm/min. (D) At drum speed of 3000 mm/min.

The instrument used to trace the time scale operates as follows: Two very light styli (A and B in Fig. 3) spaced 4 mm apart trace the base lines. The upper stylus (A) is struck from above by an impactor (C) at a rate of five impacts per sec. Every fifth impact is heavier than the others. This results in the tracing of a longer line than the others. Thus 1-sec division lines are traced, each divided by four shorter lines representing 1/5-sec intervals. These lines extend downward from the upper base line. The lower stylus (B) is struck from below by another impactor (D) at a rate of one impact in 10 sec, each sixth impact being heavier than the others. Thus 1-min division lines are traced, each minute being divided into six divisions of 10 sec each. These lines extend upward from the lower base line. The adjustment is such that the 1-min and 10-sec divisions align exactly with the corresponding 1-sec division lines. The impactors are operated by cams (E and F) driven by a small self-starting synchronous motor. The accuracy of

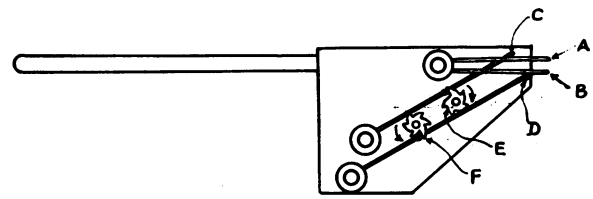

FIG. 3. The new interval timer for kymograph recording, as seen from the rear with cover removed.

[1] I am grateful to Dr. Warren H. Yudkin (now at Cambridge University, England) for pointing out the inconveniences of older methods and for requesting a solution of the problem, and to Dr. Edgar J. Boell of Yale University for making available to me facilities for testing the timer and for his helpful advice.