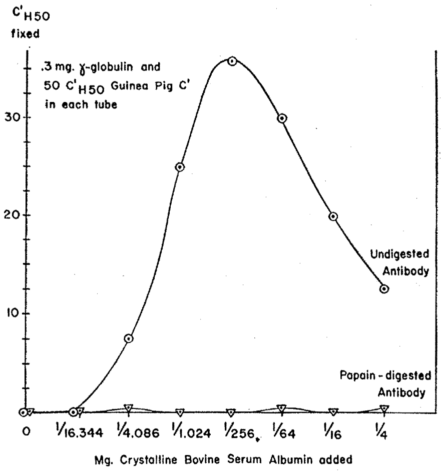

Fig. 1. Quantitative complement fixation at 4°C for 18 hours in 10 ml total volume.

first, was obtained by experiments with 5*S* antibody fragments, which are bivalent and precipitate with the homologous antigens, and comprise fragments I and II, but lack fragment III of Porter. The 5*S* fragments were prepared by means of pepsin digestion, according to the method of Nisonoff (*10*), from the rabbit antibodies previously mentioned.

Quantitative complement fixation tests done over the same wide range of antigen concentration failed to show complement fixation by the 5*S* antibody fragments. No complement fixation was detected even when the concentration of the fragment was increased 5 times over that of native antibody which was able to fix 40 of 50 50-percent hemolytic units. Addition of the chromatographically separated fragment III (*4*) from normal rabbit gamma globulin failed to restore the complement-fixing

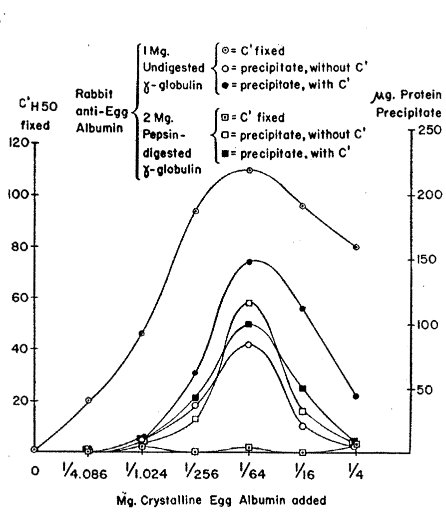

Fig. 2. Quantitative complement fixation and precipitation at 4°C for 18 hours in 3 ml total volume, with and without 200 units of guinea pig complement.

capacity of these 5*S* antibody fragments.

To study more closely the relationship between specific precipitation and complement fixation, the amount of the precipitates and the loss of hemolytic complement in the supernatants were determined in the same test tubes after 18 hours' incubation at 4°C (with 3 ml total volume). Large amounts of complement were used, which allowed determination of complement fixation not only by the decrease of the ability of the supernatants to lyse sensitized red cells, but also by the increase in the amount of precipitates.

A representative experiment is illustrated in Fig. 2. In the absence of complement, the amounts of precipitate obtained with 2 mg of gamma globulin of the 5*S* preparation are greater than those obtained with 1 mg of undigested gamma globulin. However, the undigested antibody fixed up to 110 of 200 50-percent units of complement, but pepsin-digested antibody fragments fixed less than detectable amounts. Moreover, complement consistently increased the specific precipitation of undigested antibody, as expected (*11*), but not the precipitation of the 5*S* fragments. The experiments thus provide two independent indications that the 5*S* fragments do not fix complement, despite specific precipitation with antigen.

It appears, therefore, that the antigen combining fragments I and II, whether separated (as in papain-digested antibody) or united (as in pepsin-digested antibody) are no longer able to fix complement. Whether this results from an alteration in the spatial arrangement of the antigen combining sites of the molecules or from the loss of certain structures in fragment III essential for complement fixation remains to be determined (*12*).

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References and Notes

1. P. Ehrlich and J. Morgenroth, "Uber Haemolysine," in P. Ehrlich, *Gesammelt Arbeiten zur Immunitätsforschung* (Hirschwald, Berlin, 1904), p. 135.
2. W. W. C. Topley and G. S. Wilson, *Principles of Bacteriology and Immunity*, G. S. Wilson and A. A. Miles, Eds. (Williams and Wilkins, Baltimore, ed. 4, 1955), vol. 1, p. 258.
3. W. C. Boyd, *Fundamentals of Immunology* (Interscience, New York, ed. 3, 1956), pp. 353, 361.
4. R. R. Porter, *Biochem. J.* **73**, 119 (1959).
5. M. M. Mayer, A. G. Osler, O. G. Bier, M. Heidelberger, *J. Immunol.* **59**, 195 (1948).
6. Z. Ovary, personal communication.
7. A. Nisonoff, F. C. Wissler, D. L. Woernley, *Arch. Biochem. Biophys.* **88**, 241 (1960).
8. D. Pressman, D. H. Campbell, L. Pauling, *Proc. Natl. Acad. Sci. U.S.* **28**, 77 (1942).
9. A. Osler, M. M. Mayer, M. Heidelberger, *J. Immunol.* **60**, 205 (1948).
10. A. Nisonoff, F. C. Wissler, L. N. Lipman, D. L. Woernley, *Arch. Biochem. Biophys.* **89**, 230 (1960).
11. P. H. Maurer, D. W. Talmage, *J. Immunol.* **70**, 435 (1953).
12. This investigation was supported by grants from the New York State chapter of the Arthritis and Rheumatism Foundation and from the U.S. Public Health Service (A-2594 and A-1431-C3), by an advanced research fellowship of the American Heart Association (to A.T.) and by a senior fellowship of the Arthritis and Rheumatism Foundation (to E.C.F.).

10 July 1961

International Geophysical Calendar for 1962

Abstract. Coordination of certain types of geophysical observations and analyses throughout the world is accomplished by the advance selection of days and intervals for such work. A committee under the International Council of Scientific Unions has issued the calendar for 1962, together with a brief explanation and examples of how it may be used in planning geophysical programs.

The International Geophysical Calendar 1962 (Fig. 1) (*1*) designates selected days and intervals for special attention for geophysical experiments and analysis during 1962 and is thus a framework for world-wide coordination. It serves mainly the branches of geophysics dealing with the earth's atmosphere in which many phenomena vary significantly during the course of a year. In some experiments, such as the routine recording of variations of the earth's magnetic field, the observational and analysis programs at observatories are normally carried out at a uniform level throughout the year; in these cases the calendar is not needed. However, in many other experiments (for example, rocket experiments), it is not practical or meaningful to carry out the same program on each and every day. Here the calendar can provide a useful mechanism for coordination: experimenters will know that their colleagues in other countries, in other laboratories, and in other disciplines will tend to carry out experiments on the days or intervals marked on the calendar. In this way, results of experiments may later be more easily and usefully compared.

In some scientific fields, international scientific organizations have made specific recommendations for programs to be done on days or intervals marked on the calendar. In others, the arrangements are informal or self-evident. Some examples are given below.

Regular World Days are intended for observations or analyses or special experiments which as a practical matter, can be carried out only about 10 percent of the time and should be spaced throughout the year. Examples in the field of ionospheric physics are oblique incidence pulse transmission and reception; absorption measurement by pulse reflection technique; extended observations of "whistlers" and very-low-frequency emissions; vertical sounding ionograms by *f*-plot, *h'*-plot, and so on; hourly reduction from ionograms of *F*-region true height parameters *hc* and *qc*.

The Regular World Days with highest priority are for similar work which can be undertaken only 1 day each month. A specific example is the program recommended by the International Scientific Radio Union (URSI) for exchange of copies of original ionograms in ionospheric vertical sounding work.

World Synoptic Intervals are intended for experiments that for practical reasons cannot be carried on continuously, but for which statistics of seasonal variations are especially needed. To simplify the calendar, the Regular World Intervals, World Meteorological Intervals, and International Rocket Weeks of past years have been combined for 1962 into one set of intervals. For the sake of the synoptic meteorological rocket programs, designated by the Committee on Space Research and the World Meteorological Organization (WMO), the intervals have been placed about a month after the equinoxes and solstices—the times of marked seasonal change in certain upper-air meteorological phenomena. During World Synoptic Intervals, meteorological rockets at a network of stations are launched at least once daily. Balloon sounding programs, either with special instruments or launchings to unusually high balloon altitudes, have been planned during these intervals. Ionospheric drift and high-atmosphere wind measurements are other examples of suitable programs for such intervals. In several disciplines, sample detailed data will provide a sampling of variations throughout the year, but with improved statistics during 1 month of each season.

Other special days marked on the calendar include the days of solar eclipses, two in 1962 and one in January 1963, when special programs may be expected to be carried out in appropriate parts of the world to study the sun and any effect of eclipses on the earth's atmosphere. Ionospheric stations customarily increase their observational programs even if the magnitude of eclipse at their location is small. Many solar-activity observatories take extra observations and issue specially detailed reports to assist in the interpretation of the geophysical effects. Also shown are days when meteor-shower activity is unusual. These include some of the important visible meteor showers and also unusual showers observable mainly by radio and radar techniques. Attention is also called to these days in case ionization produced by meteors may account for unusual effects in other geophysical experiments. The Annual World Meteorological Day, selected as 23 March (not marked on the calendar), was first celebrated in 1961. Its purpose is to make the services which national meteorological services can render to economic development, as well as the activities of the World Meteorological Organization, better known and appreciated by the people of all countries.

Special intervals not appearing on the calendar—periods of great magnetic, auroral, and ionospheric disturbance are also of considerable geophysical interest. World-wide coordination of observation is especially useful for stations not near the auroral zones, that is, places where the beginning of a major disturbance may not be immediately apparent from local observation. Notices of Geophysical Alerts and Special World Intervals are distributed by telegram or radio broadcast on a current basis by the solar-geophysical Regional Warning Centers, whose telegraph addresses are as follows: AGIWARN WASHINGTON (U.S.A.), DEMPA KOKUBUNJI (Japan), NIZMIR MOSCOW (U.S.S.R.), IONOSPHARE DARMSTADT (G.F.R.) or GENTELABO PARIS (France) or AGI NEDERHORSTDENBERG (Netherlands). The meteorological telecommunications net-

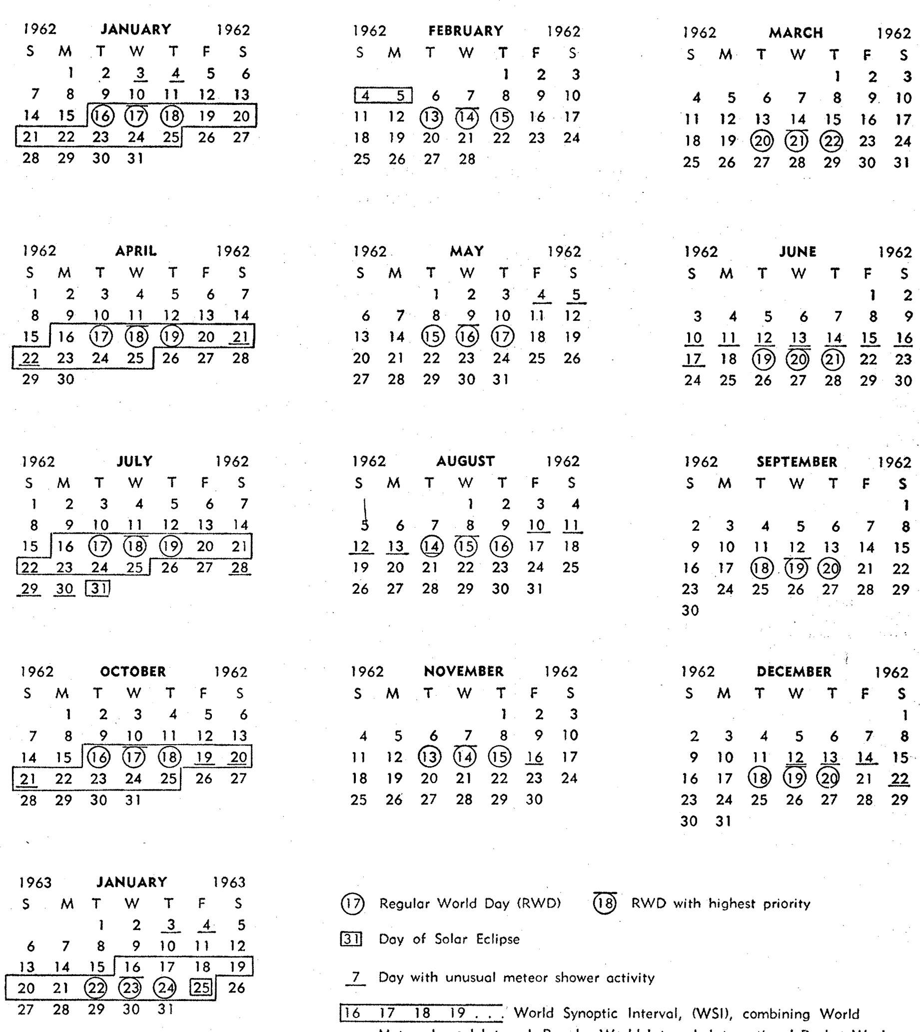

Fig. 1. International Geophysical Calendar 1962. The calendar was issued October 1961 by the International World Day Service under the auspices of the International Scientific Radio Union.

work coordinated by WMO carries such information once daily soon after 1600 U.T. Many geophysical stations increase their programs or carry on special experiments during disturbed periods. Prompt notification of immediately significant geophysical observations and of major solar flare events, which have important and sometimes long-lasting geophysical effects, are also undertaken through the Regional Warning Centers.

The International World Day Service was established in 1958 by the International Council of Scientific Unions (ICSU) and is administered by the International Scientific Radio Union, 7, Place Emile Danco, Brussels 18, Belgium. This calendar has been drawn up by A. H. Shapley and J. V. Lincoln in consultation with interested unions and committees of the ICSU and representatives of the WMO (*2*).

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References and Notes

1. Copies of the calendar are available upon request to the Secretary General, International Scientific Radio Union, 7, Place Emile Danco, Brussels 18, Belgium.
2. A more complete description of the calendar has appeared in the *U.R.S.I. Information Bulletin* and other widely available scientific publications. See also, A. H. Shapley, "International geophysical calendar for 1961," *Science* **132**, 1941 (1960).

2 November 1961

Vaccinia Dermal Infection and Methylcholanthrene in Cortisone-Treated Mice

Abstract. Cortisone-treated mice were inoculated with vaccinia virus, and then five paintings of methylcholanthrene were applied over the site of inoculation. In 70 percent of the mice, tumors developed at the site of inoculation, and 35 percent of the mice, with and without skin tumors, also developed lymphomas. Identically treated control mice that were vaccinia-immune developed a significantly lower incidence (38 percent) of both skin tumors and lymphomas.

F. Duran-Reynals (*1*) showed that in cortisone-treated mice inoculated with vaccinia virus into skin previously painted with methylcholanthrene (MC), tumors developed at the site of inoculation. In these experiments the mice received the following: first, ten MC paintings; next, cortisone to enhance the skin response to the virus, because mice are naturally resistant to vaccinia infection; and last, the virus, which was inoculated into the painted flank. Skin ulcers developed at the site of inoculation and healed within 3 weeks, forming a hyperplastic scar. Several weeks later tumors, frequently malignant, developed at the site of the scar in 66 percent of the mice.

Table 1. Different types of neoplasia in mice that received cortisone, vaccinia virus, and MC and in identically treated control mice that were vaccinia immune.

Neoplasia	Mice with neoplasia (No.)	
	Experimental	Control
Papilloma	5	2
Carcinoma	10*	3
Sarcoma	9†	6
Lymphoma	6	3
Total‡	30 (34)	14 (36)

* Two of this group also developed lymphomas.
† Four of this group also developed lymphomas.
‡ The total number of mice included in each group is shown in parentheses.

The procedure was reversed in the present experiments. That is, cortisone-treated mice were first inoculated with the virus, and then MC was applied over the site of inoculation. Results similar to those previously reported (*1*) were obtained with much less MC. The tumors appeared much earlier, grew faster, and were mostly malignant. In addition, a high incidence of lymphomas was observed, particularly in the absence of skin tumors. Mazurenko (*2*) has shown that a high incidence of lymphomas develops late in life in mice inoculated with vaccinia virus shortly after birth.

We used the following materials and methods: noninbred albino female mice, 16 weeks of age; the Levaditi strain of neurovaccinia grown in rabbit testes (infective titer for the rabbit skin 10^{-9}); cortisone (cortone acetate) injected subcutaneously in the groin (1 mg in 0.1 saline daily for 5 days). On the day of the last cortisone injection, the virus or an extract from normal rabbit testes was inoculated intradermally in the flank (0.1 ml of a 1:10 saline suspension). Beginning 24 hours after inoculation, 1-percent 3-methylcholanthrene in benzene or benzene alone was painted over the shaved back and flanks daily for 5 days. The mice were observed until death, when routine autopsies were performed (*3*).

Nine groups of about 40 mice each were used in the experiment. The experimental group received cortisone, virus, and MC. The results from the control groups were as follows. Cortisone and virus together or alone, in the absence of MC, induced no significant changes in the mice. Cortisone and MC or MC alone, in the absence of the virus, induced an incidence of neoplasia significantly lower than in the experimental group. Essentially the same results were obtained in vaccinia-immune control mice that received cortisone and virus and, 1 month later, received more cortisone, a second virus inoculation, and MC.

To avoid repetition, only the results from the experimental and vaccinia-immune control mice will be summarized in detail. Skin ulcers developed at the site of virus inoculation in all the experimental mice. Beginning 3 weeks after treatment, in 50 percent of the mice the virus-induced lesions showed a series of changes, such as extensive, confluent hyperplasia followed by chronic ulceration, which led to the development of malignant skin tumors. In the remaining mice the virus lesions healed rapidly forming a hyperplastic scar. Skin tumors also developed at the site of the scar in 20 percent of the mice. Thus, 3 months after treatment skin tumors had developed in 70 percent of the experimental mice and in only 16 percent of the control mice. When the experiment was terminated, neoplasia—skin tumors and lymphomas—had developed in 88 percent of the experimental mice and in 38 percent of the control mice.

The number of mice with different types of neoplasia is shown in Table 1. The number of mice with carcinomas and lymphomas appears to be significantly lower in the control group. Lymphomas developed in 25 percent of the 24 experimental mice with skin tumors and in none of the 11 control mice with skin tumors. The small size of the control group may account for this difference. In the case of mice without skin tumors, however, the size of the experimental and control groups was approximately reversed, and lymphomas developed in 60 percent of the smaller group of ten experimental mice and in only 12 percent of 25 control mice. These results have been shown to be consistently reproducible.

The results suggest that the chance of malignancy may be significantly increased in a host exposed to MC during vaccinia infection. The role that nonspecific factors, such as the skin injury and tissue repair, may play in these results is being investigated (*4*).

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