tions about oral contraceptives. There was concern about prediabetic symptoms in over one-third of the women. The effect of the steroids on the liver function could be serious when the nutritional level was low and where there was parasitic infestation. It was difficult to promote oral contraception mass campaigns in developing countries when the pill was still subject to medical prescription in the advanced countries.

M. C. Shelesnyak (Interdisciplinary Communications Program) called for more enterprise both in research and application. In no other field of pharmacology were the safety demands so exacting and indeed unreasonable—complete reliability of the method and no side-effects being expected. The population problem was so serious that some degree of calculated risk must be taken.

The discussions ranged over the effects of the rate of population increase not only on amenities but on the environmental necessities for survival, over the possible role of legislation in imposing either incentives or sanctions, and on communications. Here it was stressed that the levels of communication and persuasion from the educated elite to the person-to-person conversion did not conform to any global blueprint. Far more had to be known about the grass-root responses or nonresponses, because in this especially intimate question people were not going to be persuaded by either international or national imperatives.

S. Zuckerman (Chief Scientific Adviser to the U.K. Government), a specialist in reproduction physiology, pointed out that all the hormonal contraceptives, in use or in clinical evaluation, were based on physiological principles known in 1935. He urged that basic researches into human reproduction should be better supported, not just likely winners. He also urged that far more should be found out about the historical patterns of population change—like investigating parish registers in Europe. In the demographic field we needed far better information about birthrates and age distribution, not only for whole countries but for localities.

While Sir Solly accepted the fact that acreages would not be the limitation of food production and that in absolute terms there would be no desperate shortages of "hard resources" in the short term of 20 to 25 years, he foresaw grave complications in the social patterns which were considerably being determined by decisions now being taken. He cited the problems of the disposal of nuclear waste from installations being projected now. He pointed out the risks involved in the modernization of agriculture. This had to be highly capitalized and mechanized, but by intensification and localization crops became more vulnerable and liable to catastrophe. He stressed the point about reproduction in the cities now producing a labor force which would stifle migration from the countryside, while the high-yield areas would mean the virtual abandonment of the low-yield areas.

He contended that we could not decide what another generation would regard or accept as a way of life. The tendency seemed to be toward huddling together, by choice, in cities. Our responsibility was to avoid squandering resources and fouling up the amenities that the next generation might want to use. He accepted the likelihood of a rise before A.D. 2000 in mean temperature through human activities, with consequent climatic effects, and he recognized the dangers of pollution. The whole story of mankind was the adaptation of the environment. Were we producing a nonadaptable environment?

Speaking as a scientist who was concerned with practical politics, he said that there were no shortcuts to the solution of the population problem. It began with individuals. The individual had to be convinced that there was a problem. Then it had to be made societal, then political, then governmental, and then executive. Government action could only reinforce or facilitate initiatives which had already been taken.

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Influenza Virus: Genetics and Control

The recent advent of the new Hong Kong strain of influenza virus, an A_2 (Asian) variant of sufficient antigenic distinctness to infect previously immune human populations, presages another influenza outbreak of pandemic proportions in the very near future. The periodic appearance of such influenza strains within cycles of approximately 10 years is a well-known phenomenon as is the tendency for these viruses to continuously undergo "antigenic drift." Public health authorities are aware of the general ineffectiveness of our present methods for coping with new strains either by vaccination or chemotherapy, vaccination against known strains being, at most, moderately effective. Also adding to the gloom of current attemps to prevent influenza outbreaks is the inability of virologists to predict the direction which the antigenic fickleness of these myxoviruses will follow. It was against this setting and mood that an informal roundtable conference on possible new approaches to the study and control of influenza viruses was held in Princeton, New Jersey, 11–12 November 1968. This meeting, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), emphasized discussions on the genetic aspects of influenza virus with the hope that new information might be gained for the effective control of the influenza virion as a disease-producing entity and for future direction of influenza research. Participation in the conference was by invitation and included the following scientists: Convener, W. Braun (Rutgers University), S. Baron (NIAID), R. Chanock (NIAID), P. W. Choppin (Rockefeller University), F. M. Davenport (University of Michigan), F. Fenner (John Curtin School, Canberra), G. K. Hirst (Public Health Research Institute, New York), E. D. Kilbourne (Cornell University), H. G. Pereira (National Institute for Medical Research, London), M. Pons (Public Health Research Institute, New York), R. W. Schlesinger (Rutgers University), E. Simon (Purdue University), R. W. Simpson (Rutgers University), R. R. Wagner (University of Virginia), P. Wright (NIAID), and N. D. Zinder (Rockefeller University). Observers from the National Institutes of Health also attended this conference.

The first and perhaps most interesting session was on the genetics of myxoviruses and paramyxoviruses. Pons led off the discussion with a review of his earlier work demonstrating that high-molecular-weight (38*S*) single-stranded RNA could be extracted from purified influenza virus (A_0/WSN). This RNA was later shown by Pons and Hirst to consist of five distinct components as

resolved by polyacrylamide gel electrophoresis. These segments ranged in size from 2.5×10^5 to 7×10^5 daltons which would suggest that they might represent monocistronic sequences of polynucleotides. Evidence was also presented (Pons) that the replicative form (RF) of influenza RNA obtained from virus-infected cells can be resolved as five components resistant to ribonuclease. These observations evoked discussion as to the actual physical state of the RNA genome within intact virions versus its intracellular form. The suggestion (Braun) that the RNA may exist in influenza particles as a single molecule but may be replicated as separate fragments appears worthy of consideration. Pons ended his discussion of physicochemical studies with recent data concerning the molecular basis for the classical "Von Magnus phenomenon"; that is, the multiplicity-dependent production of incomplete, noninfectious influenza virus. Analyses of radiolabeled virus by gel electrophoresis showed that the incomplete form of virus contained the same protein components as fully infectious virus, but that it lacked one of the five RNA components. It will be of obvious interest to determine what genetic function or functions this missing RNA segment can perform in intact genomes.

Frank Fenner has long advocated the use of conditional lethal mutants for circumventing the technical problems that have hampered genetic studies of animal viruses. One could scarcely doubt the usefulness of this approach when considering the work discussed by Fenner on temperature-sensitive (*ts*) mutants of influenza virus, strain WSN. These data, many derived from a recent doctoral dissertation (J. Mackensie), showed that a genetic map can be constructed with influenza *ts* mutants providing that conditions for recombination are highly standardized including treatment of cells with *Vibrio cholerae* neuraminidase. Sixteen *ts* mutants of WSN virus were first ordered along a linear map that showed reasonable additivity and a maximum recombination frequency of 12 percent. However, to resolve the discrepency of lower-than-expected recombination between the terminal mutants a circular map was constructed which Fenner stressed as being quite tentative. For unexplained reasons attempts were not successful to obtain complementation between these *ts* mutants which differed from one another for various defects. Hirst discussed recent recombination studies

with similar *ts* mutants of WSN originally isolated by Simpson and Hirst and he was able to group nine nonreverting mutants within a linear map giving a maximum distance of 13 percent. Except for the suggested circular arrangement of the genetic map obtained in Fenner's laboratory it was obvious that fairly good agreement existed between these two independent sets of data.

The writer (Simpson) opened a discussion on heterozygosis with a presentation of recent results suggesting that, with some crosses between influenza (WSN) *ts* mutants, some clones presumptively classified as ts^+ or "wild-type" recombinants are probably segregating heterozygotes. It was suggested (Zinder) that most of the influenza "recombinants" obtained from crosses with *ts* mutants might be heterozygotes rather than true recombinants, similar to the events detected in crosses involving amber mutants of bacteriophages (fl). Some participants pointed out that good evidence for the occurrence of true recombinants of the influenza virus exists. However, since the very high recombination frequencies (10 to 13 percent) of influenza *ts* mutants remain unexplained (considering genome size), it is not at all inconceivable that either genetic or replicative heterozygotes could account for this anomaly by exaggerating and masking true recombination frequencies. Evidence was also presented (Simpson) that stocks of the influenza *ts* mutants contain a large proportion of virus that is noninfectious but genetically competent in recombination.

The genetics of paramyxoviruses was discussed by Simon who presented data from a dissertation (J. Dahlberg) on *ts* mutants of Newcastle disease virus (NDV). These workers performed complementation tests with 48 *ts* mutants that fell into eight or nine groups although there was strong clustering within a single group. While segregation analyses or other tests for heterozygosis were not carried out, it was concluded that recombination did not occur ($<5 \times 10^{-5}$) with these mutants and that all "ts^+" clones were actually complementing heterozygotes. Simon presented evidence that populations of NDV are heterogeneous with regard to their ploidy, many particles incorporating more than one genome. The occurrence of ploidy and heterozygotes among myxoviruses (influenza) and paramyxoviruses (NDV) has long been recognized but it is apparent that their full significance in genetic interactions is yet to be evaluated.

Pereira closed the discussion on genetic recombination with a review of his work on interaction of human and avian strains of influenza A virus. Using the technique of cross reactivation, it was shown that reactivation of fowl plague virus with different human strains of influenza resulted in transfer of the genetic determinants for neuraminidase protein of the helper virus (noninactivated human serotypes). The polygenic nature of these determinants was suggested. The final discussion topic of the genetics session involved the recent work of Chanock and associates concerning progress in the development of vaccine strains employing attenuated *ts* mutants of various respiratory agents including respiratory syncitial virus (RS), rhinoviruses, and even *Mycoplasma pneumoniae*. The desirability of isolating such mutants with presumed affinity for localization in the upper respiratory tract, where they should be capable of stimulating local production of IgA-type antibodies, was suggested by the finding that circulating antibodies actually exert an adverse effect in the case of infections evoked by RS virus. The successful isolation of several *ts* mutants of these respiratory agents was described (Chanock, Perkins, Steinberg). One now awaits an experimental confirmation that such mutants will be as useful as one might anticipate. Appearance of virulent revertants may be precluded by selection of appropriate mutants under conditions where multiple mutations are almost certain to have occurred.

The session on the biosynthesis of influenza virus and its components was disappointing in the sense that no new data became available shedding light on some of the enigmas surrounding the replication of these viruses, such as the nature of the actinomycin-sensitive, host-controlled functions. Pons reviewed his earlier work showing that actinomycin D blocks formation of the influenza replicative form of RNA. It was suggested (Braun) that some insight into this problem might be gained if the influence of agents stimulating nucleic acid synthesis (for example, by oligonucleotides) were investigated. Zinder suggested that a more critical examination of the effect of protein inhibitors, added late in the infection cycle, on viral RNA synthesis might be warranted. Interesting new findings concerning the surface structural proteins of influenza virions from studies of

Laver and the late R. Valentine were presented by Fenner. The influenza hemagglutinin protein purified by electrophoresis (cellulose acetate) could be identified as a structure with a sedimentation coefficient of 7.5*S* and measuring 40 × 140 Å. The neuraminidase protein (8.5*S*) was structurally more complex and consisted of a 40-Å (diameter) knob, a tailpiece measuring 100 Å in length and a crosspiece between these structures (50 × 85 Å). These highly purified proteins retained their antigenic specificity. While the number of nonstructural proteins that are coded for by the influenza genome is not known, preliminary data from work carried out with *ts* mutants was given (Fenner) which suggested that a minimum of 5 nonstructural antigens can be detected (3 hours) in virus-infected (WSN) cells by appropriate immunofluorescent techniques. Discussion of the proteins of influenza virus ended with a brief summation (Kilbourne) of experimental evidence supporting the concept that viral neuraminidase is instrumental in the release of mature virions from the host cell.

The final session of this conference was spent on a consideration of the epidemiological aspects of influenza outbreaks and methods for their control. Davenport gave the epidemiologists' viewpoint regarding the antigenic variation of the influenza group and its significance in the appearance of new serotypes. Pereira reported that surveillance of various domestic birds and animals revealed a high incidence of influenza infections and the viral isolates exhibited a wide range of antigenic variation. Influenza is believed to be equally rampant among wild animals that are presently being tested. It was suggested that such epizootics may constitute reservoirs of influenza strains that can undergo abrupt antigenic changes (mutation and selection) culminating in pandemic infections of nonimmune human populations. This is certainly not an unreasonable hypothesis. The apparent difficulty in constructing any laboratory model capable of predicting future antigenic changes in myxovirus populations was emphasized. It was also pointed out that there is as yet, regrettably, no adequate experimental model for assessing selective values of competing old and new strains.

Methods suggested for the possible control of influenza virus centered primarily on the use of vaccines. Kilbourne advocated the use of antigenic hybrids prepared in the laboratory for vaccination programs and the development of a repository of such strains was considered. As a case in point, it was indicated that it was recently possible to obtain a recombinant of the new Hong Kong strain with high growth capacity in eggs by cross reactivation with egg-adapted influenza virus (PR8). The chief advantage of this approach is that it circumvents the problem of securing high-titered stocks of nonattenuated field strains for use in vaccine production.

Techniques for improving the antigenicity of influenza virus or its components were also mentioned. Among them was the use of methylated bovine serum albumin (Braun) which has already been shown by Plescia and Braun to neutralize influenza virus infectivity and to be highly successful in stimulating antibody production with a number of relatively poor nonviral immunogens. Baron presented rather convincing evidence that protective levels of interferon can be induced in animals treated with double-stranded polyinosinic:polycytidylic acid complexes (PI:C) before or after challenge with such viruses as herpes simplex [*Science* **162**, 811 (1968)]. PI:C was also effective in affording protection against respiratory infection in mice exposed to A_2 influenza virus. Some toxic effects that appear to accompany PI:C treatment in certain animals may, however, preclude the immediate practical application of this approach for preventing human infections in other than topical therapy. The session concluded with a discussion of future needs in influenza virus research.

Undoubtedly much of the success of the conference can be ascribed to the choice of the convener, Werner Braun, whose strong background in the genetics of microorganisms and unbiased interest, as an "outsider," in the biology of influenza virus infections were responsible for the valuable contributions that he made in the discussion of various topics. The meeting ended on the note that serious gaps still exist in our knowledge of the genetics of the influenza virus. Hopefully, these gaps may be bridged by new approaches, particularly by a more intense utilization of recent physico-chemical and genetic methods discussed at this conference.

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Calendar of Events

Courses

Fundamentals of Dynamic Measurements as Applied to the Ocean, San Diego, Calif., 11–14 March. Is designed for practicing engineers, scientists and technicians who use sophisticated electronic instrumentation in ocean research. The course will enable the participant to gain a firmer knowledge of the instruments necessary to perform measurements of time-varying phenomena as they apply to the ocean sciences. Will include units on recorders, signal generators, transducers, analog and digital conversion, waveforms, filters, amplifiers, voltage regulators, and the ocean research applications of these units. (Third Ocean Sciences Short Course, Instrument Society of America, Education and Research Services, 530 William Penn Place, Pittsburgh, Pa. 15219)

Infrared Spectroscopy, Cambridge, Mass., 17–27 June. This course is intended for chemists, biologists, and medical research workers who wish intensive training in the methods of infrared spectroscopy and interpretation of infrared spectra. The course covers infrared instrumentation and techniques (1 week) and applications to problems of chemistry and biology (1 week). Tuition $500 for both weeks, $275 for either week alone. Tuition scholarships for academic personnel. (Dr. Richard C. Lord, Director, Spectroscopy Laboratory, Massachusetts Institute of Technology, Cambridge 02139)

Desalination: Methods and Applications, Berkeley, Calif., 24–28 March. The course is planned as an introduction to desalination and a survey in depth of the state of the art, covering the development, theory, application, and economics of the principal methods of desalination, including separation by phase change, reverse osmosis, and electrodialysis. The registration fee is $275. (Continuing Education in Engineering, University of California Extension, Berkeley 94720)

Water Pollution Control, Bronx, N.Y., 2–6 June. Two one-week courses, supported jointly by Manhattan College and the Federal Water Pollution Control Administration, will be offered for advanced study in "Stream and Estuarine Analysis" and "Biological Waste Treatment." The fee for each course is $175. Stipends and travel allowances are available for United States citizens associated with universities and state regulatory agencies (Donald J. O'Connor, Civil Engineering Department, Manhattan College, Bronx, N.Y. 10471)

Contemporary Optics, Rochester, N.Y., 28 July–8 August. Both the fundamentals of optics and their application to problems and developments in contemporary optical research and engineering will be discussed. In order to have a cohesive course that will provide a broad coverage of optics, the subject matter has been divided into four sections: quantum optics, Fourier optics, geometrical optics, and optical physics. Tuition is $500 for applications received by 15 June and $525 thereafter. (Contemporary Optics, Institute of Optics, College of Engineering and Applied Science, University of Rochester, Rochester, N.Y. 14627