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Editor's Note

The very positive reaction that welcomed the publication of *Biology International* indicates that the IUBS News Magazine is meeting a real need among the large international biological sciences community and expresses the deep interest of the international scientific societies and national scientific institutions in the Union's objectives, programmes and activities.

Consequently, due to the encouragement received, and in order to develop and promote this channel of communication, an Editorial Board has been appointed for *Biology International*, composed of active members of the Union representing the various disciplines of biological sciences and the different fields of interest of the IUBS.

*Biology International*'s feature articles will focus on topics of general interest to biologists such as the search for new tools for Biology, Biology and Society, Biological Education and Training... and to serve as an open forum for presenting and discussing controversial themes in biological sciences.

In addition, it will report regularly and systematically on the scientific programmes and activities of the IUBS major components and on the other Bio-Unions and Committees of the ICSU family.

Finally, *Biology International* will continue to provide useful information on the main events, meetings and publications in the field of International Biology.
Short Term Tests to Assess the Mutagenic and Carcinogenic Hazards of New Chemicals

by Professor Nicola Loprieno, Laboratory of Genetics, University of Pisa, Via S. Maria, 53, 56100 Pisa, Italy.

1. INTRODUCTION

The increasing number of synthetic compounds in the human environment has given increased relevance to toxicology: among other fields, environmental mutagenesis or genetic toxicology has been greatly developed during recent years, due to the discovery that several possible long term genotoxic deleterious effects (mutagenic/cancerogenic) might have been produced by chemicals in man, such as vinyl chloride, anesthetics, etc.

Extensive mutagenic investigations on different indicator laboratory organisms (bacteria, fungi, insects, mammalian cells in culture, mice, hamsters, rats, plants, etc.) developed so far, have demonstrated that many of the chemicals in common use are able to induce mutations in one or several genetic systems of different biological organization.

According to the Chemical Abstract Service, some 4, 039, 907 distinct chemicals were present in the CAS's Register in November 1977: the number was growing at an average rate of about 6,000 compounds per week, and therefore the list should today include more than 5,000,000 chemicals.

The best estimate of chemicals in common use is 63,000 ca. compounds, according to the U.S. Environmental Protection Agency and the U.S. Food and Drug Administration, distributed in the classes reported on Table 1.

Table 1
Classification of chemicals in common use to which the general population may be exposed.

<table>
<thead>
<tr>
<th>Class of compounds</th>
<th>Number estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemicals in every day use</td>
<td>50,000</td>
</tr>
<tr>
<td>Active ingredients in pesticides</td>
<td>1,500</td>
</tr>
<tr>
<td>Active ingredients in drugs</td>
<td>4,000</td>
</tr>
<tr>
<td>Compounds used as excipients</td>
<td>2,000</td>
</tr>
<tr>
<td>Food additives</td>
<td>2,500</td>
</tr>
<tr>
<td>Chemicals used to promote life</td>
<td>3,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>63,000</strong></td>
</tr>
</tbody>
</table>

To date, as many as 20,000 compounds have been tested for their genotoxic potential activity: it is now possible, by means of several indicator organisms employed in the laboratory, to classify those chemicals found mutagenic into compounds producing different types of DNA alterations of known molecular nature, or into compounds producing somatic and/or germinal mutations. On the basis of these differential results, it is also possible to define qualitatively and/or quantitatively the mutagenic or the genetic risk following human exposure to the chemicals.

These data have focused our attention on the possible genetic hazard for exposed human population and have greatly influenced the researches on chemical mutagenesis.

In the past, during the 1960's, the research emphasis in mutagenesis was concerned with the effects of ionizing radiation: in this case an increase of potential human contamination by radiation was considered when many studies had elucidated the types of damage produced at the level of DNA and organism. Such knowledge has been constantly used to limit and control the spreading of radiation contamination of the human environment. Great efforts have been devoted therefore, to the development of efficient safety procedures able to protect the general public from casual radiation exposure.

The present situation of chemical contamination of the human environment is still almost completely out of our control, due to the fact that the possible number of chemicals which can be produced is so high that it is practically indefinite. In addition, our present biological laboratory resources do not allow the rapid screening of the mutagenic potential of all the compounds to which the general public might be potentially exposed.

A large fraction of the human population is currently exposed to the chemicals. A reduced fraction of it, the workers, is chronically exposed to effective doses with potential genotoxic activity: it is, however, extremely difficult at present to identify single individuals or a large population whose genetic structure could have been altered by environmental mutagens.

Moreover, it is still not possible to establish safety measures for many chemicals, whose genotoxic potential activity has not yet been analyzed.
The only road to a rational control, i.e. the limitation of those chemicals particularly effective as genotoxic agents, is the development of effective guidelines which can evaluate potential mutagenic chemicals to be spread or employed in our environment.

The present aim of environmental mutagenesis is the application of already existing mutagenic methodologies in the evaluation of new compounds.

The methodologies so far developed, vary in their complexity and in their informative value, according to the genetic system under consideration and the test organism used in the methodological procedure.

Mutagenicity tests of practical use do exist among those so far available, and those which may represent the basis for a real control of environmental mutagenic agents can be selected and recommended for extensive use.

Some present legislative attempts at national or international levels do correspond to the need indicated by scientists to develop a better control of the quality of human life.

"It is quite possible and even probable that the overall effect of all these chemicals, acting separately or in combination, may be a far greater genetic hazard than that posed by ionizing radiation. It is the inescapable duty of geneticists to assess this hazard as accurately as possible, of governments to lay down guidelines for the clearance of substances for use, and of industry to follow these guidelines and collaborate in the testing. All this is, indeed, under way" (AUERBACH, 1976).

2. ENVIRONMENTAL MUTAGENESIS AND GENETIC DISEASES

The researches developed in the last 10-20 years have defined the genetic basis of more than two thousand human pathological syndromes (MC KUSICK, 1979): they are caused by autosomal dominant, autosomal recessive and X-linked genes which account for a total of 10.1 x 10^-3 cases of live birth. Moreover, a total incidence of 6.1 x 10^-3 cases of live born babies with chromosome abnormality (sex or autosomal trisomy, or structural chromosome rearrangements) has been ascertained by several cytogenetic programmes developed in different international laboratories. For some known chromosomal abnormalities present at the birth, as in the case of double Y syndrome (47, XYY), Klinefelter syndrome (47, XXX), Triplo X syndrome, Turner syndrome (45, XO), Trisomy of the 21st chromosome (Down syndrome of the 18th, and of the 13th chromosome, the values of the relative incidence are known and they range between 1 : 970 for (47,21 + ) to 1 : 7,500 for (45, XO).

These chromosomal abnormalities are produced during maturation of gametes of both sexes and are due to the mechanisms known as chromosomal nondisjunction. The latter does not allow a separation of the chromosomes of a pair during meiosis, when the diploid chromosome number is reduced to half. Although the direct evidence shows that part of these chromosomal defects are due to the age, a large fraction of them might be due to exogenous environmental factors of chemical and physical nature.

According to data collected by WHO, the results show that 15% of all pregnancies do terminate early (spontaneous abortions): the cytogenetic studies have demonstrated that some fifty per cent of them are the result of other types of chromosomal abnormalities.

All these data (live born and spontaneous abortion) indicate that chromosomal mutation in human population is in the order of \(26.47 \times 10^{-2} \times \text{gamete} \times \text{generation}\).

In a total of 10,000 pregnancies, therefore, we may calculate the values reported in table 2, which express the incidence of cases with some type of genetic alteration (lethals + live born).

Table 2: Incidence of gene and chromosomal alterations among human pregnancies

<table>
<thead>
<tr>
<th>Type of abnormality</th>
<th>No cases : 10,000 pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Single gene alteration</td>
<td>101</td>
</tr>
<tr>
<td>B. Chromosomal abnormality</td>
<td>61</td>
</tr>
<tr>
<td>C. Spontaneous abortion (due to chromos. defects)</td>
<td>687</td>
</tr>
<tr>
<td>Total</td>
<td>849</td>
</tr>
</tbody>
</table>

Roughly 8.5% of all pregnancies, therefore, are represented by some kind of genetic alteration which is, for the majority, incompatible with the life (7.0% cases and that a value of ca. 2.0% give rise to malformed child or to a child affected by a genetic disease.

A relationship between a genetic disease and the spread of chemical mutagens in the human environment has not been established. However, "we may judge that four fifths of our ambient mutation rate is of environmental origin and could be eliminated by environmental hygiene (relating to drugs, food additives, and possibly some natural foods, water and air pollutants, certain virus infections). About 10% of that quota can be attributed to the natural radiation background, which is essentially not avoidable, and an equal proportion to artificial radiation" (LEDERBERG, 1972).

Another support to the hypothesis that genetic diseases in human population could have occurred, at least in part, to environmental mutagenic chemical factors, derives from some of the recent researches developed in the field of environmental mutagenesis: the types of mutation which have been experimentally produced in the laboratory animals or human cells grown in vitro reflect those genetic alterations which have also been observed in humans (figs. 1 and 2), as a result of gene mutations or chromosomal mutations.

We are, therefore, concerned that a possible increase of the present incidence of genetic diseases in human population should be avoided as it might reflect the development of uncontrolled mutagenic environment: on the contrary, if any type of control is not defined, there might be a real possibility for a future genetic disaster in the human population.
GENETIC RISKS FROM POINT MUTATIONS
AN EXPOSURE TO A CHEMICAL MUTAGEN OF:

1. (1) human or mammalian cell grown "in vitro"
   produces
   MUTATIONS AT LOCI WHICH CONTROL BIOCHEMICAL FUNCTIONS
   f.i.: HGPRT"; TK"
   MUTATIONS AT LOCI WHICH CONTROL RADIATION SENSITIVITY
   f.i.: Xer. pigm. osum
   At. telangiectasia
   recessive
   recessive
   dominant
   PHENOTYPIC MUTATIONS
   BIOCHEMICAL MUTATIONS
   SKELETAL MUTATIONS
   Handicapped individuals

Fig. 1
(From LOPRIENO, 1980)

GENETIC RISKS FROM CHROMOSOME MUTATIONS
EXPOSURE OF dd MICE TO A CHEMICAL MUTAGEN:

produces

IN FERTILIZED ♀♂ MICE
f.i.: Dominant lethal
F₁ EMBRYONIC DEATH DUE TO THE PRESENCE OF CHROMOSOME MUTATIONS IN SPERM CELLS

IN F₁ PROGENIES REDUCED FERTILITY AND F₂ ZYGOTIC DEATH DUE TO THE PRESENCE OF TRANSMITTED TRANSLOCATIONS
f.i.: Heritable translocations

Fig. 2
(From LOPRIENO, 1980)
3. OBJECTIVES OF MUTAGENIC TESTINGS

Genetic researches aimed at a better understanding of the role of the environment on the incidence of human genetic diseases, have developed a number of experimental procedures for studying the mutagenic effects of chemical compounds present in the human environment. These methodologies vary in their complexity and in their informative values, according to the genetic system under consideration and the test organism used in the methodological procedure.

The most relevant mutagenicity tests for defining the genetic risk for man, by a chemical mutagen, employ small laboratory animals (e.g., mice). In this case, the aim of the mutagenicity tests that have been developed is to determine:

(a) whether the chemical substance induced a mutagenic effect which can be transmitted to the progenies of exposed individuals;

(b) the type of mutagenic effect induced on the basis of the genetic significance for the progeny (point or gene-mutation; chromosomal mutation);

(c) the frequency of the induced mutations in the progeny of the exposed animals.

Such tests present a high reliability, since by themselves they can establish not only the mutagenic properties of a chemical compound, but also the importance of these effects for assessing the potential genetic risk for man of a given compound. The present mutagenic methodological assays which use mammals as a test organism, are, for many, very costly and require long experimental periods. Further development in this field of genetic toxicology will provide the most practical test systems.

Due to its intrinsic interest, genetic research has developed investigations into biological organisms and on biological phenomena involved in the functions of genetic material: these studies have provided a long list of mutagenic methodological assays which are easy and rapid to handle. Using these studies it is possible to investigate some important biological properties developed by a chemical agent.

In this way, numerous short-term tests have been so far developed by which it has been possible to define the ability of a chemical agent to produce:

(a) a hereditary mutation consisting of an alteration in the molecular structure of the gene;

(b) an alteration in the structural organization of a chromosome, or in the numerical organization of a genomic structure;

(c) an increase in recombination between different genes or between the two alleles of the same gene which are present in a heterozygous individual.

These three phenomena are the direct consequence of the initial reactions which a chemical agent produces on the cellular DNA of an organism. Moreover, these three types of phenomena are irreversible and their genetic nature can easily be unequivocally demonstrated in the majority of cases, so that a 100% correlation can be established between the type of effects and reactions with cellular DNA, with absolutely no possibility of error.

With such short-term tests it is possible to establish in absolute terms whether a chemical agent is mutagenic in that particular experimental system: the sensitivity of these mutation tests also allows for the detection of the minimal effective concentration or dose at which mutations occur with a frequency significantly different from that of events occurring spontaneously. Moreover, by using these systems, it is possible to define the quantitative dose-effect relationships with a high level of significance. This then gives us an indication of the kinetics of the reactivity that a chemical agent possesses towards the important cellular constituents.

The short-term tests consist of prokaryotic and eukaryotic unicellular organisms and include bacteria (Salmonella typhimurium, Escherichia coli, etc.), yeasts and fungi (Saccharomyces cerevisiae, Schizosaccharomyces pombe, Neurospora crassa, Aspergillus nidulans, etc.). In some of these organisms (e.g., yeasts and fungi) and in addition to gene-mutations, it is also possible to evaluate recombination phenomena, and numerical chromosome normalities such as nondisjunction. Other organisms used in this type of evaluation are mammalian cells grown in vitro, on which it is possible to determine the ability of a chemical compound to produce gene and chromosome mutations, and, moreover, other biological reactions (Sister Chromatid Exchange; Unscheduled DNA Synthesis, etc.). Since, with this type of cell it is possible to study directly in vitro at the level of the mammalian genome structure phenomena, such as gene mutations and chromosome mutations, it is generally thought that results obtained by evaluating the chemical agents on these mutagenicity tests are of greater relevance in the assessment of the genetic hazard of the chemicals.

Other whole organisms, such as Drosophila melanogaster, whose genetic knowledge is of a high level, provide several methodological assays for assessing the ability of a chemical agent to produce all kinds of genetic effects.

At present, in order that mutagenicity tests become a reliable tool for the evaluation of the genotoxicity of a class of chemicals, the following conditions must be fulfilled:

(a) the genetic system must be well characterized and allow expression of the greatest possible number of mutational events, even of different molecular types, the genetic system used is maintaining its pattern of response to a number of reference mutagens,

(b) the methodological procedure for evaluating the mutagenic potential of a chemical agent must allow for all the conditions, which are essential for expression of the biological reactivity of the compounds;

(c) the analytical and experimental system must enable a quantitative assessment of the effect to be evaluated, in relation to the exposure dose;

(d) the inclusion of a metabolising system, when the test organism or the cell system does not itself possess the metabolic capacities of the mammals. In this case the experiments must be conducted with and without supplementary provision for these capacities;

(e) the methodology used must be corroborated by an extensive series of experiments confirming its applicability to chemical agents belonging to structurally different classes;
(f) the results obtained should be evaluated using statistical methods appropriate to the test used; should be based on replicate experiments; and on a size of the treated and control samples which are large enough to ensure that a negative result in a test has a statistical meaning;

(g) the evaluation of a possible chemical mutagen should provide enough evidence that ancillary components of the mutagenicity test (solvents, cofactors, microsomal preparation, etc.) are not themselves mutagenic or contaminated with mutagens.

At present there are several methodologies for performing short-term mutagenicity tests: they are reported in tables 3, 4 and 5.

Table 3
Organisms and genetic test systems for the assessment of gene mutations induced by chemical compounds.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Genetic system</th>
<th>Genetic end point</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. BACTERIAL TESTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. <em>Salmonella typhimurium</em></td>
<td>A. Rev. Mutat.</td>
<td>Base-pair changes</td>
</tr>
<tr>
<td>2. <em>Escherichia coli</em></td>
<td>A. Rev. Mutat.</td>
<td>Base-pair changes</td>
</tr>
<tr>
<td><strong>B. YEAST TESTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. <em>Schizosaccharomyces pombe</em></td>
<td>A. Forw. Mutat.</td>
<td>Base-pair changes</td>
</tr>
<tr>
<td><strong>C. FUNGAL TESTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. <em>Neurospora crassa</em></td>
<td>A. Forw. Mutat.</td>
<td>Base-pair changes</td>
</tr>
<tr>
<td>2. <em>Aspergillus nidulans</em></td>
<td>A. Forw Mutat.</td>
<td>Base-pair changes</td>
</tr>
<tr>
<td><strong>D. MAMMALIAN CELLS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. AZA-Resistance V-79</td>
<td>A. Forw. Mutat.</td>
<td>Intragenic mutations</td>
</tr>
<tr>
<td>2. TK Mutation L5178Y</td>
<td>A. Forw. Mutat.</td>
<td>Intragenic mutations</td>
</tr>
<tr>
<td><strong>E. INSECTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>F. MAMMALS</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1. Mouse specific Locus test | A. Rec. Mutat. (Forw. Mutat.) | Intragenic mutat. | &
| 2. Mouse spot test * | A. Rec. Mutat. (Forw. Mutat.) | &                                       |
| 3. Sperm abnormality * | A. Rec. Mutat. (Forw. Mutat.) | Small Deletions                         |
| **G. HOST MEDIATED ASSAY** | Forw. Mutat. Rev. Mutat. | The same as in A.B.C.D.                 |

* Tests not well validated, difficult to perform, or organism requires additional genetic characterization.
Organism and genetic test systems for the assessment of chromosome mutations induced by chemical compounds.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Genetic system</th>
<th>Genetic end point</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. MAMMALS</strong> (in vitro)</td>
<td>A. Periph. blood lymphocyte</td>
<td>Chrom, aberrations</td>
</tr>
<tr>
<td></td>
<td>B. Somatic cell line</td>
<td>Chrom, aberrations Sister Chrom. Exchange (SCE)</td>
</tr>
<tr>
<td><strong>B. MAMMALS</strong> (in vivo)</td>
<td>A. Micronucleus</td>
<td>Somat. chrom. aberrat.</td>
</tr>
<tr>
<td></td>
<td>B. Bone marrow cells</td>
<td>Somat. chrom. aberrat.</td>
</tr>
<tr>
<td></td>
<td>C. Germ cell cytogen.</td>
<td>Germ cell chromos. aberrat.</td>
</tr>
<tr>
<td></td>
<td>D. Dominant lethal</td>
<td>Herit. chromos. aberrat.</td>
</tr>
<tr>
<td></td>
<td>F. Somatic cell</td>
<td>Sister chrom. exchange (SCE)</td>
</tr>
<tr>
<td><strong>D. YEASTS &amp; FUNGI</strong></td>
<td>A. Mitotic recomb.</td>
<td>Chrom. rearrangements</td>
</tr>
<tr>
<td></td>
<td>B. Gene conversion</td>
<td>Gene rearrangements</td>
</tr>
<tr>
<td></td>
<td>C. Non-Disjunctions</td>
<td>Genome mutations</td>
</tr>
</tbody>
</table>

Organisms and test systems on which other biological effects are relevant for the assessment of mutations induced by chemical agents.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Type effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. BACTERIAL TEST</strong></td>
<td>Cell lethality due to absence or repair processes.</td>
</tr>
<tr>
<td><strong>B. YEASTS &amp; FUNGI</strong></td>
<td>Phenomena (mitotic recombination &amp; gene conversion) related to repair processes.</td>
</tr>
<tr>
<td><strong>C. SOMATIC CELL</strong> (in vitro &amp; in vivo)</td>
<td>Sister Chromatid Exchange (SCE) as indicator of repair processes. Unscheduled NDA Synthesis (UDS)</td>
</tr>
<tr>
<td></td>
<td>A. Autoradiography</td>
</tr>
<tr>
<td></td>
<td>B. 3H-TdR incorporation in the DNA</td>
</tr>
<tr>
<td></td>
<td>C. DNA breaks evaluation</td>
</tr>
</tbody>
</table>

4. METABOLIC ACTIVATION AND DETOXIFICATION: INDIRECT MUTAGENS

One of the main reasons for the difficulty in using the in vitro mutagenicity tests for the evaluation of chemical agents and for the extrapolation of the data for assessing the genetic risk for man, resides in the complexity of metabolic activation/detoxification reactions to which foreign chemicals are submitted in human tissues. The membranes of the liver cell endoplasmic reticulum, for instance, hydroxylate numerous exogenous compounds by a multimolecular system known as the mixed function oxidase. This system carries out several metabolic reactions including:

(a) nitro-reductions;
(b) N-dealkylations;
(c) O-dealkylations;
(d) S-dealkylations;
(e) epoxidations;
(f) dechlorinations;
(g) alcohol oxidations.

The role of cytochrome P-450 in these metabolic reactions and its inducibility by several xenobiotic compounds has been extensively demonstrated. All these metabolic reactions, moreover, require participation of other enzymatic systems and co-factors, such as NADPH, NADH, NAD, O₂, reduced glutathione, glucuronate, UTP, UDP-G, and ATP. They are all important factors, as interference or depletion of one or more of them may cause uncontrolled release of “activated” epoxide intermediate to the immediate intracellular component.

The complexity of pathways by which several xenobiotics can be activated is presented in Fig. 3: such a scheme may provide insight into the complexity of the multienzymatic reactions which xenobiotic compounds undergo in vitro, thus producing electrophilic metabolites which are usually eliminated by means of detoxication mechanisms (conjugation or hydration), but which possess an extremely high reactivity towards genetic material. From Fig. 3 it is possible to understand why depletion of conjugation cofactors, such as glutathione and glucuronide, would minimize detoxication pathways and allow increased covalent binding.
Many environmental contaminants have been shown to be subjected to liver mixed-function oxidase systems, and to be transformed into reactive mutagenic metabolites. They include haloalkanes, haloalkenes, halocaromatic compounds, dimethylnitrosamine and various polycyclic aromatic hydrocarbons. Species, sex, age, diet, habits, genetic differences, previous environmental exposure, exposure to compounds with hormonal activity, and other factors yet unknown modulate the response of individuals to chemical agents in their environment.

Other factors which may influence the genetic risk following exposure to a chemical are represented by polycyclic hydrocarbons in tobacco smoke, consumption of charcoal broiled meat, peroxidized fats, and food products containing xenobiotic compounds. Other chemicals are transformed into mutagenic metabolites by the intestinal microflora; in some cases, such as that of cycasine, β-glucosidase enzyme transforms the original compound into an aglycone. Recently it has been shown that extracts prepared by some bacterial strains isolated from human faeces are mutagenic for *Salmonella TA 1525* strain; this result indicates that some intestinal microbes can also convert certain dietary components to mutagens *in vivo*.

The knowledge of all these metabolic reactions has made possible the development of suitable *in vitro* or *in vivo* methodological procedures for assessing the potential activity of those chemicals which are subjected to a metabolic conversion by mammalian enzymatic reaction.

*In vitro* tests which include post-mitochondrial microsome supernatant preparation (S-9) to which cofactors or pure liver microsomal preparations are added have been developed; for the same reasons, various types of host mediated assays have been developed: the latter combines a microbial genetic test system, with an *in vivo* metabolic system (a treated mammal is inoculated with a microbial cell population, on which the mutagenic potential of the chemical agent is assessed).

It has been indicated that the degree of responses of many mutagens when tested, (on *Salmonella typhimurium*) might depend on as many as fourteen different factors, shown as follows:

(a) choice of tester strain;
(b) choice of test protocol: plate incorporation, liquid culture fluctuation, host mediated;
(c) choice of organ from which the S-9 mix is prepared (usually liver);
(d) choice of species from which the liver S-9 mix is prepared;
(e) choice of liver enzyme-inducing agent: Aroclor 1254, 3-methylcholanthrene, phenobarbitone, folic acid deficient diet, or non induction;
(f) the volume of S-9 mix used and the balance therein between S-9 fraction and co-factors;
(g) addition of purified enzymes to the S-9 mix, or depletion of enzymes through sub-fraction of the initially derived S-9 fraction;
(h) addition of non-mutagenic adjuncts, such as norharman or nitro-sarcosine, to the assay medium;
(i) the time of incubation of the bacteria with the test chemical;
environmental factors: 80% of cancer deaths are due to environmental factors of different types (pollution, influence, etc.).

The degree of responses of other mutagens when tested on yeasts might depend on the pH during treatment, the phase growth of the cells (logarithmic or stationary), and the temperature during incubation, etc.

The degree of responses of some mutagens when tested on mammalian cells grown in vitro might depend on the expression time, pH, etc.

Other factors which may influence the in vitro metabolic mutagenic evaluation are represented by the type of pharmacokinetics which might lead to the formation of a highly reactive or highly insoluble metabolite that is unable to pass the membrane barrier of the cellular system for different reasons; or by a very slow metabolic conversion so that the length of time of microsomal preparations are used in vitro renders evaluation unreliable, or a multistaged metabolic conversion in which the stage specific for production of the mutagenic metabolite is one of the last steps; or because there is a requirement for enzymes which are not present in the microsomal preparations. Among these problems, a recent one is represented by those compounds which require plant metabolic activation and do not respond to the normal in vitro mammalian metabolic activation system, although they seem to be mutagenic in vivo, in the intact animal (i.e.: atrazine) (LOPRIENO, 1980).

5. MUTAGENIC AND/OR CARCINOGENIC CHEMICALS

Cancer is the second cause of human death whose influence may well increase in the future due to environmental factors: 80% of cancer death is due to environmental factors of different types (pollution, nutrition, drug therapy, etc.). Among these factors, chemical substances are highly represented, as it has been demonstrated the positive correlations between hundreds of them and their ability to produce cancer in animals and man: 26 different chemical substances or mixtures have been classified by the International Agency for Research on Cancer, a WHO institution, as human carcinogenic factors. Highly represented among human carcinogens (18/26) are chemicals which are contaminants of the working environment.

During recent years, on the basis of the developed researches on chemical reactivity of several compounds towards biological systems with the aim to define the mechanism of action of carcinogenic chemicals, the chemical carcinogenesis has become highly relevant and it has stimulated further studies on the relationship between the carcinogenic process and other biological processes.

The basic structure of a cancerogenous cell is mainly represented by its incapacity to follow the homeostatic equilibrium of cells in animal tissues, as they undergo cell cycle divisions. All these new properties are inherited by all deriving cells: therefore a genetic mechanism responsible for the change in a cancerous cell has been widely proposed and accepted. In several cases, it is possible to demonstrate the clonal origin of the cancerous cells, as in the case of idiopathic myelofibrosis, multiple myeloma, chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, idiopathic chronic cold agglutinin disease, etc.

All these data have allowed to put forward the hypothesis of the mutational origin of cancerous cell, which might arise as a consequence of even more than one mutational event. According to Mc Farlane Burnet (1974), each cellular mutational event in the carcinogenic pathway confers a proliferative advantage to a mutated cell on the non mutated cells present in the population.

Independently from its origin, each tumor presents, in all cells, an altered genetic informational program different from the original one and therefore it is possible to accept the idea that all new biochemical, cytogenetic and proliferative properties of the cancerous cells might well be the result of one or several somatic mutations. It is, moreover, possible to suppose that the carcinogenic process is the result of a series of different alterations occurring on the genetic material of a cell or of viral genes present in the cellular genome: these alterations may be either the result of genic or chromosomal mutations or the result of a different genetic mechanism which provides the cell with a different genetic structure (gene-conversion and/or somatic gene-recombination).

According to this theory, the role of chemical agents in the production of different types of somatic mutations, seems highly relevant, as a preliminary and prerequisite stage of the evolution of a normal cell to a cancerous one.

Many of the chemical compounds have a reduced polarity and accumulate principally in the fat tissue of the organism: by means of different metabolic reactions, as those indicated in the previous section, they are converted in polar structures which may then undergo a series of chemical reactions with macromolecules, such as DNA or RNA. In the majority of cases, the metabolic conversion of an inactive compound (pro-carcinogen) transforms it into an intermediate and finally into an ultimate carcinogenic compound. It has been extensively demonstrated that metabolic conversion is able to transform an inactive compound into an electrophilic structure which is by then able to form a duct with nucleophilic sites present in nucleic acid molecules: the formation of a $0^{-}$ alky guanine with miscoding property has been proved to be responsible for mutation in different organisms and the initiation process in the neoplastic transformation (fig. 4).

A valid support of the hypothesis that carcinogenic compounds are also mutagens has been produced by the data collected by McCANN et al. during 1975-1976 in a series of chemical mutagens/carcinogens tested on the bacterium Salmonella typhimurium (Ames test): according to these results the Ames test can identify about 90% of carcinogens (sensitivity of the test) and can reject, on the basis of
negative results about 87% of non carcinogens (specificity of the test) (Fig. 5): although the validity of this assumption resides in the percentage of carcinogens present in the sample of chemicals analyzed, on the chemical nature of the analyzed chemicals, and on the metabolic reactions, several other studies have demonstrated that these results are generally valid (Table 6). The best current estimate of the ability of the Salmonella test to identify chemical carcinogens as mutagens indicates a value in the range of 70-80%.

Other short-term mutagenicity assays may, however, be combined with the Ames test to improve the predictability of mutagenicity tests.

A recent programme developed by different institutions has shown how feasible the possibility actually is of identifying the carcinogenic chemical compounds by several different mutagenic assays.

Although there are limitations to the use of short-term mutagenicity tests \textit{in vitro} assays in the assessment of carcinogenic compounds (which depends on several factors, as, for example those indicated in Table 7), the use of mutagenicity tests has proved to be the only practical possibility for the evaluation of thousands of chemicals present in the human environment as a prescreening method for carcinogenic compounds.

At present, short-term tests for chemical carcinogens do not constitute definitive evidence as to whether a substance does represent a carcinogenic hazard to humans. However positive results indicate suggestive evidence for a carcinogenic hazard: therefore short-term mutagenicity tests are useful in a prescreening programme for identification of potential carcinogenic chemicals.

6. THE NEED FOR A BATTERY OF TESTS

As previously stated, there are two ways of altering the genetic material, namely the production of the gene-mutation and the alteration in the structural organization of a chromosome or in the numerical organization of a genome's structure; other types of genetic effects, such as recombination and gene conversion may, moreover, represent some genetic risk, as these could allow the expression of recessive harmful mutations present in a heterozygous individual. For the above reasons, a comprehensive system of evaluation of chemical compounds should be based on the use of assay test procedures which are representatives of:

(a) a variety of biological organization (single cell and multicellular organisms);
(b) a variety of ultimate genetic effects, including all types of genetic alterations;
(c) a variety of initial molecular events at the DNA level.

With radiation, all kinds of genetic effects are produced in different experimental test organisms; very few chemicals, on the contrary, produce as many different types of genetic alterations as X rays. Results of mutagenicity tests developed with different mutational assays have, to some extent, demonstrated the presence of specificity of the mutagenic activity: Natulan, Bleomycin, Urethane, Auramine, O-Toluidine, Ethionine, 1, 2-Dimethylhydrazine are mutagenic in some genetic tests but not in others. Since, in the future, there is no direct possibility of implementing the present available mutational systems at an absolute value of 100% efficiency level for reason of specificity, there will always be compounds capable of inducing or of not inducing mutation in any particular genetic and cellular system. This also, because there is no sufficient experimental demonstration at present capable of predicting whether compounds identified as false positive or false negative in a mutational system will also be found as such in another mutational system.

For these reasons, the need for a battery of tests has been recognized either to confirm positive data and, or to minimize the frequency of false negative data. The use of biological systems with different genetic organization may, however, produce con-
Contrasting differential responses, depending on the particular genetic end point being evaluated and the cellular organization considered. For instance, a chemical might produce a negative response in a test for point mutation induction, and a positive response in a test for chromosome aberration induction. It is very often possible to explain contrasting results between different biological systems in which genetic end points of the same nature are analyzed. The reasons might be due to a peculiar kinetics of the metabolic conversion of the compound; the need for a particular error-prone repair process; or the existence of a cell-stage specificity.

These problems also indicate the need of some interpretation of data, before making a conclusive decision about the genotoxicity of a chemical agent: in the case of contrasting results, both the relevance of the negative data to the definition of the mutagenic potential of the genetic risk, and of what consequence they are to inadequate test procedures applied in the evaluation of the compound, should be taken into consideration.

Any screen for mutagenicity should include two types of tests for each of the two main types of genetic effects, namely one test for point-mutation and one for chromosome-mutation: Each test should provide the evidence that the substance, or its metabolite, does not result in mutagenicity, when a large range of non toxic and sub-toxic concentrations are assayed on the test organism.

In order to minimize the possibility of the false positive or false negative, an additional test may be required for both types of genetic effects, developed on organisms or genetic systems different from the previous test. Since other biological cellular reactions are easy to test and have demonstrated a great sensitivity and a higher specificity, it could be relevant to develop, besides the four tests, an additional test for assaying the possible influence of the chemical substance on repair reactions: this result may give more additional useful information, especially if the test is performed on a type of cell with a high nuclear organization.

At the moment, there is no satisfactory information showing one type of tests to another as more preferable. There are, however, some types of tests which have had a large diffusion, thus allowing the development of data base, which are of great relevance to the problem of understanding comparative results, both at chemical structure level, as well as at the level of the possible metabolism of the class of compounds. The Salmonella typhimurium 4 or

<table>
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<tr>
<th>Author</th>
<th>Chemicals analyzed</th>
<th>Carcinogens</th>
<th>Non carcinogens</th>
</tr>
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<tr>
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<td>300</td>
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<td>B. COMMONER (1976)</td>
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<td>T. SUGIMURA et al. (1977)</td>
<td>241</td>
<td>85,0</td>
<td>26,0</td>
</tr>
<tr>
<td>M.M. BROWN et al. (1979)</td>
<td>52</td>
<td>84,0</td>
<td>25,0</td>
</tr>
<tr>
<td>H.S. ROSENKRANZ and L.A. POIRIER (1979)</td>
<td>87</td>
<td>51,7</td>
<td>16,6</td>
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<td>V.F. SIMMON (1979)</td>
<td>87</td>
<td>63,7</td>
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<tr>
<td>H. BARTSCH (1979)</td>
<td>180</td>
<td>76,0</td>
<td>43,0</td>
</tr>
</tbody>
</table>

(*) False positive. (From LOPRIENO, 1980).
more strains is such type of test: it has been extensively applied to thousands of compounds; other short-term mutagenicity tests have been developed to a high standard and have been applied to hundreds of chemical compounds.

Table 7

Factors that determine the processes of cancer development in vivo and are not duplicated by mutagenicity systems

1. Biological absorption and distribution.
2. The concentration of ultimate reactive metabolites available for reactions in organs and animal species with cellular macromolecules.
3. The biological half-life of metabolites.
4. DNA repair mechanisms between the test system and the whole animal.
5. Immunosurveillance.
6. Organ-specific release of proximate or ultimate carcinogens by enzymatic deconjugation.
7. Deactivation reactions which can lead to compounds possessing either no carcinogenic activity or less carcinogenic potential than the parent compound.

7. LEGISLATIVE ACTIONS AND RECOMMENDATIONS

During the last five years, legislative actions have been made with the aim to control the spread of new mutagenic/carcinogenic chemicals in the human environment.

On October 11, 1976, the Toxic Substances Control Act (TSCA) was issued in USA "to regulate commerce and protect human health and the environment by requiring testing and necessary use restrictions on certain chemical substances, and for other purposes". In Section 4, this law requires that the new chemicals should be tested for their potential carcinogenesis and mutagenesis among other properties.

As an example of the application of this new law, guidelines for testing pesticides or chemical industrial compounds have been proposed by the US Environmental Protection Agency in the Federal Register (August 22, 1978 and July 26, 1979 respectively).

In Europe, a sixth amendment was issued by the European Communities on Sept. 18, 1979 (No 79/831/EEC), namely Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances: this law prescribes pre-manufacturing notification (contrary to the TSCA, which prescribes pre-manufacturing notification) of new chemicals. It regulates and indicates how many tests should be developed to assess, among the other properties, the potential mutagenicity and carcinogenicity of new chemicals.

Action is in progress, at the moment, to define these two laws, as well as several national laws on the same argument and the type of the tests that should be performed, in order to evaluate the potential mutagenicity.

In order to harmonize the legislative decisions in all countries, attempts have been made at a supranational level to issue recommendations on the tests required. The Organization for Economic Cooperation and Development (OECD), which is composed of 24 industrialized western countries, is preparing the principles for the evaluation of the mutagenic carcinogenic potential of chemicals.

A recent document by OECD states that a valid scientific approach to the evaluation of chemicals for mutagenicity can employ tests utilizing prokaryotic and eukaryotic mutational systems: these tests should be used to generate data for pre-marketing of the new chemicals.

For the Minimum Premarket Data Set (MPD), the OECD recommendation states that it is necessary to obtain information on two categories of endpoints, gene (point) mutations and chromosomal aberrations.

As a part of the MPD on new chemicals, it will generally be necessary to obtain:

1. Information on the production of gene (point) mutations in prokaryotic cells such as Salmonella typhimurium. Experimental evidence indicates that Escherichia coli is also suitable.
2. Information on the production of chromosomal aberrations preferably in appropriate mammalian cells grown in vitro. An in vivo procedure, e.g., the micronucleus test and metaphase analysis of bone marrow cells, is also acceptable. Only one test in each of the above categories needs to be conducted to fulfill the requirements of the MPD.

If, for scientific and/or technical reasons, the application of the suggested tests is not possible, evidence from different tests could be presented in the MPD. It is recognized that evidence derived from other tests could have equal validity and thus be accepted as an alternative to part of the MPD set. However, scientific reasons should be provided to demonstrate that such data is as good as can be expected from the recommended tests.

When unavoidable exposure to the chemical of relatively large numbers of people, or involuntary exposure to the chemical of the general population, is expected, additional mutagenicity testing may be required to confirm the results observed in the MPD, or to elucidate potential genetic hazard indicated from the results of earlier mutagenicity tests.

The first series of tests (at confirmation level) is represented by:

a. Gene mutations
   (1) eukaryotic microorganisms
   (2) mammalian cells
   (3) sex-linked recessive lethal (Drosophila)
   (4) mouse spot-test

b. Chromosomal aberrations
   (1) in vivo cytogenetics-somatic cells (e.g. micronucleus and bone marrow) and/or germlinal cells (e.g. spermatogonia)
   (2) dominant lethal in rodents.
Tests to elucidate the genetic hazard are represented by:

a. Gene (point) mutations
   (1) Mouse specific locus test
b. Chromosome mutations
   (1) Heritable translocation test.

Besides all these rather specific tests with definite genetic end point of known biological mechanisms, there are several other tests which are indicators of genetic toxicity: these may be complementary to previous mutagenicity tests and may assist the interpretation of other mutagenicity tests. The tests include:

(1) DNA damage and repair in bacteria;
(2) DNA damage and repair in mammalian cells;
(3) Sister chromatid exchange;
(4) Sperm abnormality test;
(5) Mitotic recombination and gene conversion in yeasts.

The OECD working group has recognized the value of short-term mutagenicity tests for their use in the prediction of carcinogenic activity. It recommends, in the screening for potential carcinogenicity, the combination of bacterial tests with all other mutagenicity tests, including indicator tests and in vitro cell transformation assays.

It has been recognized that a positive result from the MPD mutagenicity tests would suggest that the chemical is a possible carcinogen and/or a potential mutagen and that, since no MPD can presently detect all genotoxic compounds, negative data generated by the tests previously indicated, should not be taken as fully definitive evidence of non-genotoxicity.

It is clear that in the OECD recommendations, all scientific conclusions are included so far derived from the literature in the field of environmental mutagenesis, i.e. those which have been discussed in previous sections.

These recommendations are now being utilized to implement the international laws, such as, the EEC Council Directive of Sept. 18, 1979.

8. CONCLUSIONS

The present scientific knowledge demonstrates the existence of thousands of chemical compounds widely used in the human population, or pollutants of the human environment which are able to directly react with the genetic material of all different types of organisms or which are metabolically converted by mammalian enzymatic systems to electrophilic structures able to interact with nucleophilic centers present in DNA molecules.

Such reactions allow these chemicals to produce mutations in the genetic structure of organisms or to initiate the cancer process into animal cells. Evidence indicates that the same mechanism is operating for producing cancer by environmental chemical factors into man; experimental data suggests that chemical mutations could explain many of the genetic human diseases.

Several methodological procedures have been developed which are able to identify mutagenic compounds, i.e. those producing gene (point) mutations and chromosomal aberrations. These short-term mutagenicity tests are also useful for the prediction of carcinogenic potential of the chemicals and may be employed in a screening programme to select the potential carcinogenic compounds.

The sensitivity and the specificity of each one of these short-term mutagenicity assays is lower than 100%: the combination of two or more of them may increase this value.

Attempts are being developed at the government level to define guidelines for testing the mutagenic/carcinogenic potential activity of new chemicals before their manufacturing or marketing, in order to avoid any further increase of such type of chemicals into human environment: they represent the efforts to transform into practical action some recent scientific concepts.

The development in the near future, of thousands of data based on this toxicological aspect would permit a confirmation of the validity of such a scientific approach in a rational control of the chemical contamination of our environment.

9. BIBLIOGRAPHY


P.L. GROVER: Chemical Carcinogens and DNA. CRC Press, Boca Raton, 1979 (2 Vol.).


J.A. HEDDLE: Genetic hazards to man from environmental agents, Mutation Res., 33, 1975.


Cell biology is now a rapidly expanding area in the biological sciences. This review gives a brief account of the formation of an international body representing cell biologists throughout the world, which developed from a small group of scientists meeting informally to exchange information. As this field of science expanded, the organisation changed to meet new conditions. The review outlines the history, aims and administration of the Federation and describes its Journal and its international Congresses.

History of the Federation

The International Federation for Cell Biology (IFCB) is the successor to a society for the study of Cytology, originally founded in 1933 and reformed in Stockholm in 1947 as an International Society for Cell Biology by 33 “founding members” who, in the first years of the recovery from a devastating war, realised the need for an international forum for a new and rapidly developing field of biology. The Society played an invaluable part in the development of cell biology, particularly in the organisation of international meetings. By the 1970’s the development of large national cell biology societies made it obvious that a federation of societies would serve cell biology better than the small international society conceived in 1947. After discussions with representatives of national cell biology societies, the International Society took the necessary steps to establish a Federation of Cell Biology Societies to which the assets of the parent Society were transferred. The IFCB was formally established at a meeting in St. Louis in 1972 by representatives of the American and Japanese Cell Biology Societies and the European Cell Biology Societies. The Indian and Canadian Societies for Cell Biology are now affiliated to the Federation and an IberoAmerican Society and a Cell Biology Society of the People’s Republic of China have now been established.

The aims of the Federation

The aims of the Federation are to promote international cooperation and to contribute to the advancement of cell biology in all its branches. The Federation sponsors an international congress every 4 years and also acts as a coordinating body which may initiate special studies and encourage research in subjects outside the normal scope of national societies, such as the problem of scientific communication.

The Federation represents cell biology in the International Union of Biological Sciences. The affiliation makes the IFCB a constituent of the International Council of Scientific Unions (ICSU) and puts our congresses officially under the aegis of the ICSU. This detail is of particular importance to colleagues in some countries in which grants for attendance at international congresses sponsored by the ICSU. The IFCB is also represented in the International Cell Research Organisation (ICRO) which functions in UNESCO.

Administration of the Federation

The Officers of the IFCB are elected by a General Assembly which meets every four years at the time of an international congress. The General Assembly consists of delegates elected by the member societies. The voting power of each delegation is determined by the size of the society it represents. The small dues paid by member societies to support the IFCB are also assessed according to the size of the societies, at rates voted at each General Assembly.

The Executive Committee consists of general secretaries (or appointed delegates) of the constituent societies, so that each society, irrespective of size, has an equal voice in the organisation. The affairs of the Federation are controlled by the General Assembly and matters
arising between meetings are dealt with by postal communication, thus avoiding expensive travel costs for business meetings. So far the Federation has been able to fulfil its functions with a minimum of organisation and at low cost.

A major function, the organisation of each international congress, is delegated to a member society which takes full responsibility for the Congress to which it plays host. When funds are available the Federation provides a block grant to the Congress organisers to help young cell biologists mainly from developing countries to attend the meetings. These funds are allocated by the Scientific committee of the Congress and the assessment is based on the scientific quality of the abstracts submitted. These grants usually cover only part of the travel costs or subsistence.

The IFCB has developed according to federal principles. It is not conceived as a powerful centralised organisation, but as an agent, through which the national and regional groups of cell biologists can act in the international sphere.

The Officers are:

President: B.R. Brinkley, Houston, USA.
Vice-President: H. Terayama, Tokyo, Japan.

The Journal of the Federation - Cell Biology International Reports.

The Federation publishes a monthly journal which was established to improve communication between scientists working in cell biology and related fields. The journal’s flexible approach encourages brevity and clarity of expression. Particular importance is given to the rapidity of publication. Standard papers normally appear within 3–4 months of acceptance. One-page papers appear within 4–6 weeks of acceptance. Apart from the space restriction, the same scientific criteria and standards of refereeing are applied to both.

The journal publishes papers describing original work on any topic in cell biology and related fields in biomedical research, applied biology, cancer, cellular immunology and pharmacology, radiobiology, etc. Papers which develop important new conclusions from published information, short reports on methods (if these contain new principles or represent technical advances of importance), and short accounts of meetings of general interest are also published. The journal is also prepared to experiment with new types of format for scientific papers. A report from each constituent society giving Officers and dates of forthcoming meetings is published in the January issue of the Journal. Each issue also includes a comprehensive list of national and international meetings of interest to cell biologists. The journal is available to members of constituent societies at a greatly reduced rate.

The International Congresses of Cell Biology

Although the International Congress of the Federation held in Boston in 1976 was the first to be held under the auspices of the new Federation, it was the 14th in a series organised by the parent organisations and by far the largest. An international congress is held every 4 years. Abstracts of all communications, including posters, are provided for each meeting but a major feature is the publication of a book, by invited participants covering most of the rapidly advancing areas in cell biology. This provides a wide ranging review of the whole field and has proved to be of great value to scientists and to students. The host for the 1st Congress was the American Society for Cell Biology. Over 5,000 scientists took part in this meeting and topics considered at plenary and other sessions included plasma membrane organisation, cell to cell interaction and communication, cell surface changes, cell structure (biogenesis of mitochondria, the endoplasmic reticulum and Golgi apparatus in plants and animal cells, microtubules and flagella, etc.), and cell movement. Sessions were also devoted to organisation and assembly of chloroplasts and somatic plant hybridisation by fusion of protoplasts. The eukaryotic cell cycle and the cytoplasmic control of nuclear expression were considered at two sessions and the structure of genetic material at other sessions on chromatin structure and function, functional organisation of chromosomes, molecular cytogenetics of eukaryotes and morphogenesis of gametes. The pathology of the cell was discussed in sessions on cell surface in neoplasia, viral gene function in cell transformation and cells of the artery wall and arteriosclerosis. All these topics are reviewed in the Congress publication “International Cell Biology 1976–77”, edited by B.R. Brinkley and Keith Porter (Rockefeller University Press).

The second international Congress was held in Berlin from August 31st-September 5th 1980. This Congress was organised by the German Society for Cell Biology acting for the European Cell Biology Organisation. There were over 3,250 participants and 1,855 scientific contributions from 50 nations. Although the pattern of the meeting was similar to that of the Boston
Congress, the emphasis differed in that there was a particular interest in molecular genetics and intra-cellular filaments. A feature at the Congress was a series of plenary lectures on "New Concepts of Gene Organisation and the Experimental Use of Defined Genes". This series covered: Organization and Reorganization of Immunoglobulin Genes (P. Ledder); Genetic Manipulation of the Embryo (K. Illmensee); Gene Mapping and Gene Transfer in Mammalian Cells (F. Ruddle); Eukaryotic Genes in Prokaryotic Cells (W. Gilbert); Chloroplast and Nucleus: Concerted Interplay between Genomes of Different Cell Organelles (D. von Wettstein).

The topics covered in a series of symposia, workshops and poster sessions were: Genomes, Transcription, RNA Processing and Associated Structures; Membranes, Protein Synthesis, Secretion and Cell Interaction; Contractile and Cytoskeletal Elements, Intracellular Movements and Cellular Locomotion; Differentiated Cells and Cell Differentiation; Special Cell Systems and General Problems of Cell Metabolism; Cell Pathology and Cellular Aspects of Disease; New Methods in Cell Biology.

The Congress publication "International Cell Biology 1980-81" edited by H.G. Schweiger is published by Springer Verlag, Berlin. A final comment based on a report from the Chairman of the Organising Committee (H.G. Schweiger) and the Secretary General (W.W. Franke) is worth repeating. "Interaction between biologists from different countries and generations can only be achieved when our younger colleagues have the chance to communicate with prominent figures from the previous generation. At large congresses most contributions must be in poster form and the results of this and other meetings show that the scientific substance is a good or better as that in platform presentations. We emphasise this point since grantgiving bodies tend to give preference to invited and platform papers. Please help to overcome this unjustified attitude".

The 3rd International Congress will be held in Japan in 1984 and the 4th in Canada in 1988.

THE IUBS EXECUTIVE COMMITTEE MEETING 1981

The 1981 Executive Committee Meeting of IUBS will take place from 29 September to 1st October 1981 to conduct the affairs of the Union as provided in Article 10b of the statutes.

In order to inform the Executive Committee of the recent work of the Union, the Secretaries of all Divisions, Sections and Commissions are kindly requested to prepare a brief summary of their activities since their 1980 report, and to send it to the IUBS Secretariat no later than 1 September 1981.

The report summaries will serve to prepare the Annual Report of the Secretary-General to the Executive Committee.

At its Meeting, the Executive Committee will examine subvention requests for 1982. It is recalled that all subventions should be formally requested whether for congresses or symposia on special forms available from the Secretariat or for the scientific activities of the Divisions, Sections and Commissions by letter giving all details on their financial situation and their action programme.

All requests should be sent to the Secretariat as soon as possible and no later than 1st August 1981. These requests have to be forwarded to the Members of the Subvention Committee in advance of the Executive Committee Meeting. Therefore, any requests which do not reach the Secretariat by the deadline of 1 August 1981 will not be taken into consideration.

Attention is drawn to the recommendation of the last IUBS General Assembly to give priority to subvention requests for interdisciplinary projects and programmes of value to developing countries.

On the other hand, the last IUBS Officer's Meeting, 27-28 April 1981, decided that subventions to be given to international biological sciences congresses will be allocated as loans and not as grants.

Under the provision of Articles 8 and 9 of the Union's By-Laws, National Committees and Scientific Member Bodies may send a representative as an Observer at their own expense. Such representatives have no voting rights, but they are welcomed to participate in discussion.
These are being written up to provide examples of the types of educational activities which are possible in this field. At the same time they are being studied in order to develop strategies for determining the biological needs of communities and for ensuring that the biological knowledge and other relevant expertise available through appropriate agencies in a community are used to meet these needs. The project is looking at the roles of research institutes, museums, health centres, the media and similar agencies, besides those of universities, colleges and schools.

Obviously the Commission hopes that the work of these projects will be of direct help in, at least, some countries. However, their main purpose is to provide examples of what can be done - and at little expense, for the projects have very limited funding. They provide examples also of the value of international co-operation in such work.

Following the London meeting, the Commission has organised further annual meetings in association with other bodies. In 1979 this was with the Institute for Science Education (IPN) at the University of Kiel, West Germany. In 1980, the Commission joined with the Asian Association for Biology Education during its biennial conference in Osaka, Japan and for June 1981 a meeting is organised in association with a conference on “Out-of-School Science Activities” being held by the International Council of Associations for Science Education (ICASE) in Singapore. Each of these meetings has been on one or more aspects of the general theme of “Biological Education for Community Development”. They provide the Commission with the opportunity to share its ideas and activities with a wider range of people and, at the same time, provide a wider than usual international perspective to the associated conference.

One particularly tangible product of these efforts has been the publication in 1980 of a book titled “Biological Education for Community Development”. It provides a unique survey of the issues involved in the topic and a review of activities from twenty countries. Other publications are likely to follow.

The Commission is much concerned with the dissemination of ideas and information. Besides the conferences and projects and their associated publications, a Newsletter is produced twice a year which currently reaches 600 people world-wide. It contains details of the publications and activities of other bodies as well as of the Commission itself. The Editor is Professor Adnan Badran, of Yarmouk University, Irbid, Jordan. Through its representation on the ICSU Committee on the Teaching of Science (ICSU-CTS) the Commission works with the Education Commissions of other Scientific Unions. The Commission’s chairman is also chairman of the Bio Unions Sub-Committee of CTS which serves to co-ordinate the work of the Commissions of other Unions with a biological interest. Among projects initiated by this group are ones on mathematics and physical science teaching for biologists and the use of computers for biology teaching. ICSU-CTS has recently developed the theme of “Science for Society” in its work which links well with the interests of the IUBS Commission. The Commission also works closely with UNESCO, and, for example, contributed to a recent meeting in Paris on “Adapting Science and Technology to Changing Societies and to the Diversity of Needs of Member States”. It is right, also, to point out that UNESCO, through its Divisions of Scientific Research and Higher Education and of Science, Technical and Vocational Education, has supported many of the Commission’s activities with grants and UNESCO personnel have provided valuable contributions to our joint efforts.

With the meeting at Singapore in June 1981 the Commission comes to the end of its present three-year plan of activities. Shorty after, we anticipate that the publications of the projects will be made available and so we are currently planning a programme for the period 1982-84, hopefully starting with a meeting in Canada in 1982 in association with the IUBS Congress. Obviously “Biological Education for Community Development” will still have relevance, but we are looking for other priorities. During a brief discussion at our last meeting, members of the Commission came up with some fourteen possibilities covering topics ranging from the relevance of technological developments to biology courses to links between the biological and social sciences, methods for practical work, examinations and assessments, new teaching methods in higher education, and the problems of linking different levels of biological education. We will have to make up our minds eventually on only a few topics because our resources are limited, but, in the meantime, if anyone would wish to offer suggestions I would be pleased to receive them.

The IUBS Commission for Biological Education
by Professor Peter Kelly, Chairman,
IUBS Commission for Biological Education,
The University of Southampton, U.K.

In the nineteen sixties and early seventies biology gained a great deal of publicity. Major discoveries and attractive new ideas in genetics, ecology, microbiology, ethology and other fields hit the headlines and made biological research popular. It also stimulated major changes in biological education. Curricula were brought up-to-date and new techniques for teaching and learning were devised. In appearance, at least, this period was, in many countries, one of extensive innovation. Today, although research does not hit the headlines so much, it is probably true to say that biology is recognised more substantially than it was previously. The reason for this is that there is greater acceptance of the fact that so many of the major problems facing people today are biological in nature. It is recognised much more that, for example, health, nutrition, population, environment and the biological technologies are fundamental to human survival and contentment, and that an understanding of biological ideas is necessary in order to contend with them. There is less interest in the spectacular research result but more appreciation of the steady benefits derived from biological work.

This emphasis on the social role of biology which emerged in the seventies has placed a fresh emphasis on the importance of biological education. Research can provide the basic means by which social problems can be dealt with but it is insufficient in itself. You require also political and administrative action; and, above all, it is necessary to provide adequate and relevant education to a wide range of people. This is, of course, particularly true of developing countries.

This change in public attitudes towards biology coincided with the establishment of the current IUBS Commission for Biological Education and has influenced its policies over the last three years. The Commission consists of 25 members appointed by the IUBS Executive. A worldwide spread of membership is ensured by having members from each of the following geographical areas: Africa, Asia and Australasia, Europe (including the USSR), Latin America and the Caribbean, the Middle East and North America. The members cover a wide range of experience both in biology and allied subjects and in educational activities. Thirteen of them come from developing countries.

The theme of the Commission's work over the last three years has been "Biological Education for Community Development". Following a meeting on the theme commissioned by UNESCO and held at Chelsea College, London in 1978, three projects were established. Each project is co-ordinated by a member of the Commission and includes other members of the Commission, together with non-members having a special interest in the topic.

One project is co-ordinated by Dr. R.A. Kille of Edinburgh University, Scotland, and is concerned with the development of short unit-courses in human biology for undergraduates. The courses include health, nutrition, environmental and other social aspects. Whilst they should clearly be of value to future biologists, the units are intended particularly for undergraduates who do not become biologists. Some, at least, of these will eventually hold administrative and other positions in a community and have a significant influence on community problems of a biological nature. It is important that they have an understanding of basic biological principles and their application to community development. The project is producing a Guide for lecturers and some illustrated materials for students. It is intended that they should provide a stimulus and advice for adaptation and further development in individual countries.

The second project, co-ordinated by Professor F. A. Gornall of the University of British Columbia, Canada, is aimed at school teachers. Initial research has been undertaken into teaching methods and the development of inexpensive and easy-to-use curriculum materials of relevance to biological education for community development, especially those for cultivating appropriate decision-making skills in pupils. This involves trials in schools in two developed and two developing countries. It is intended to produce a teachers' manual and some resource materials for use particularly in pre-service and in-service teacher education.

The third project is co-ordinated by Dr. M. Atchia of the Mauritius Institute of Education. Its concern is community education. Case studies of community-based activities involving biological education have been undertaken by members of the project in different countries.
As reported in the two previous issues of Biology International, a scientific Conference-Exhibit on the topic "Ecology in Practice: establishing a scientific basis for land management" will be held at Unesco Headquarters in Paris from 22-29 September 1981. A three-day session of the International Coordinating Council of the Man and Biosphere (MAB) Programme will follow from 30 September - 2 October. These three events will mark ten years of the MAB Programme.

The scientific conference, jointly organized by Unesco and ICSU, will focus on concrete field activities where an attempt has been made to conduct ecological research which responds to development needs. The conference is based on invited papers and a summary of the conference programme and confirmed speakers is given in the Box below.

Scientists interested in participating in the conference, at their own expense, should contact: Francesco di Castri, Division of Ecological Sciences, Unesco, Place de Fontenoy, 75007 Paris.

Summary of conference programme and confirmed speakers:

- **Tuesday 22 September**
  Theme 1: The search for sustained production systems in the humid and sub-humid tropics
  Moderator: A. Gomez-Pompa
  Review paper: F. Golley

- **Wednesday 23 September**
  Theme 2: Scientific basis for the management of grazing and marginal lands
  Moderator: F. Boulière
  Review paper: M. Ayyad & G. Long

- **Friday 26 September**
  Theme 4: Ecological approaches for improving urban planning
  Moderator: P. Zaremba
  Review paper: S. Boyden
  Other contributors: L. Sanchez de Carmona, A. von Heuler, H.A. Andrews, K. Newcombe, O. Ianitski, Y. Friedmann

- **Saturday 26 September**
  Theme 5: Use of scientific information for environmental education purposes
  Moderator: A. El-Hili

- **Monday 28 September**
  Theme 6: Providing the types of information needed for decision-making on land management
  Moderator: H. Sene
  Contributors: M. Holdgate, B. Messerli, A. Whyte, J. Jeffers, R. Baker

- **Tuesday 29 September**
  Theme 7: Emerging issues and priority problems for the 1980s
  Moderator: Didin Sraptopradja
  Combining the strengths of governmental and non-governmental approaches: M. Dooge
  Overview of main results of the Conference: R. Slatyer

#### ASSETS

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and Banks</td>
<td></td>
</tr>
<tr>
<td>Petty Cash in Fr. Fr.</td>
<td>51</td>
</tr>
<tr>
<td>The Chase Manhattan Bank - Frankfurt Main in US $</td>
<td>62,604</td>
</tr>
<tr>
<td>The Chase Manhattan Bank - Paris in US $</td>
<td>5,672</td>
</tr>
<tr>
<td>The Chase Manhattan Bank - Paris in Fr. Fr.</td>
<td>984</td>
</tr>
<tr>
<td>Amro Bank Utrecht in Dutch Guilders</td>
<td>4,490</td>
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<tr>
<td>Deposit Account - Paris, in US $</td>
<td>52,056</td>
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<tr>
<td><strong>Total Assets</strong></td>
<td><strong>125,857</strong></td>
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<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other Assets</td>
<td></td>
</tr>
<tr>
<td>Marketable Securities (market value 12,058)</td>
<td>13,881</td>
</tr>
<tr>
<td>Other receivables</td>
<td>2,110</td>
</tr>
<tr>
<td>Loans</td>
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<tr>
<td><strong>Total Other Assets</strong></td>
<td><strong>25,991</strong></td>
</tr>
<tr>
<td><strong>Less : Liabilities</strong></td>
<td></td>
</tr>
<tr>
<td>Sundry Creditors</td>
<td>13,646</td>
</tr>
<tr>
<td><strong>Excess of Assets over Liabilities</strong></td>
<td><strong>138,202</strong></td>
</tr>
</tbody>
</table>

### Statement II. Income and expenditure accounts for the year ended December 31, 1980 in US Dollars)

1. **Income**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
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</thead>
<tbody>
<tr>
<td>ICSU/UNESCO Basic Allocation</td>
<td>8,000</td>
</tr>
<tr>
<td>ICSU Subvention</td>
<td>5,000</td>
</tr>
<tr>
<td>UNESCO grants for Scientific Meetings</td>
<td>19,614</td>
</tr>
<tr>
<td>Contributions from National Members</td>
<td>164,577</td>
</tr>
<tr>
<td>Interest and Dividends</td>
<td>5,942</td>
</tr>
<tr>
<td>Gain on Exchange</td>
<td>(1,175)</td>
</tr>
<tr>
<td>Other income</td>
<td>747</td>
</tr>
<tr>
<td><strong>Total Income</strong></td>
<td><strong>202,705</strong></td>
</tr>
</tbody>
</table>

2. **Expenditure**

   A. Meetings

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Committee Meeting</td>
<td>14,190</td>
</tr>
<tr>
<td>Officer’s Meeting</td>
<td>8,121</td>
</tr>
<tr>
<td>Representation at Meetings</td>
<td>11,933</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>34,244</strong></td>
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</tbody>
</table>

   B. Publications

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>12,976</strong></td>
</tr>
</tbody>
</table>

   C. Scientific Activities

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grants to Scientific Meetings</td>
<td>14,989</td>
</tr>
<tr>
<td>Support Scientific Activities</td>
<td>41,200</td>
</tr>
<tr>
<td>Contributions to other Scientific Organizations</td>
<td>5,937</td>
</tr>
<tr>
<td>Re-Organization Committee</td>
<td>8,465</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>70,591</strong></td>
</tr>
</tbody>
</table>

   D. Administrative Expenses

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offices of the President and Secretary-General</td>
<td>2,000</td>
</tr>
<tr>
<td>Salaries</td>
<td>47,220</td>
</tr>
<tr>
<td>Related charges</td>
<td>30,512</td>
</tr>
<tr>
<td>General Office expenses</td>
<td>14,146</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>93,878</strong></td>
</tr>
</tbody>
</table>

   E. Other

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bank charges</td>
<td>451</td>
</tr>
<tr>
<td>Audit fees</td>
<td>2,801</td>
</tr>
<tr>
<td>Other expenses</td>
<td>3,052</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>214,741</strong></td>
</tr>
</tbody>
</table>

**Excess of Income over Expenditure**                             | **(12,036)** |
**Accumulated balance brought forward**                           | **150,238**  |
**Accumulated balance carried forward**                           | **138,202**  |

21
BIOLOGICAL EDUCATION FOR COMMUNITY DEVELOPMENT
Edited by P.J. Kelly and G. Schaefer (191 pages).
This book presents a collection of papers and comments from the two workshops organized by the IUBS Commission for Biological Education at Chelsea College in the University of London 1978 and at the Institute for Science Education (IPN) at the University of Kiel (FRG). It is a unique document in that it contains information and ideas on the subject from a truly international perspective.

BIOLOGICAL EDUCATION NEWSLETTER
No's 5 and 6.
Published by the IUBS Commission for Biological Education.
The two issues include reports on the Commission's activities and especially on the joint meeting with the Asian Association for Biological Education (AABE) on "Biological Education for the Next Decade" 27 October - 1 November 1980, Osaka - Japan.

BIOLOGICAL CONTROL IN ORCHARDS, BIOLOGY AND CONTROL OF CODLING MOTH
West Palearctic Regional Section Bulletin (WPRS) of the IUBS Section of Biological Control 1980 (88 pages).
This bulletin reports on two meetings held at Wye, 25-29 March 1980 by the working groups on integrated control in orchards and codling moth of the International Organization for Biological Control - West Palearctic Regional Section (IOBC - WPRS).
It contains the results of biological control research on the red spider mite, leaf-curling midge and codling moth.

BREEDING FOR RESISTANCE TO INSECTS AND MITES
WPRS Bulletin of the IUBS Section on Biological Control 1981 (115 Pages).
This volume contains 29 papers presented at the meeting on the Working Group on Breeding for Resistance to Insects and Mites held at Maidstone, U.K. from 9 - 11 April 1980. They cover a wide variety of arable, vegetable, fruit and fodder crops.

DISTRIBUTION DES FOURMIS DU GROUPE FORMICA RUFA EN EUROPE
WPRS - IUBS Section of Biological Control
Five maps on the distribution of Formica species in Europe (F. rufa L., F. Pratensis Retz., F. Polycynta Först, F. Lugubris Zett and F. Aquilonia Yarrow) have been prepared by Professor G. Ronchetti of the Institute of Entomology, Pavia University (Italy).

INTEGRATED PROTECTION IN ORCHARDS
WPRS Bulletin of the IUBS Section on Biological Control 1980 (60 pages).
This issue presents the results of the meeting in French and Spanish of the Working Group on Integrated Control in Orchards concerning Pear Insects : results and perspectives, held at Zaragoza (Spain) from 22-24 April 1980.

ENVIRONMENTAL PROTECTION AND BIOLOGICAL FORMS OF CONTROL OF PEST ORGANISMS
In Ecological Bulletins No. 31 published by the Swedish Natural Science Research Council, Editorial Service, Box 23136, S 10435 Stockholm, Sweden.
Edited by B. Lundholm and M. Stackerud, this volume is based on the papers presented at the Symposium on "Environmental Protection and Biological Control of Pest Organisms" 14-17 May 1979, Stockholm Sweden, organized by the Swedish Commission for Research on Natural Resources and the Swedish Products Control Board, with the aim of assessing present knowledge of the risk aspects of biological controls.