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EXPERIMENTAL GENETICS AND HUMAN EVOLUTION

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Planning based on informed foresight is the hallmark of organized human intelligence, in every theater from the personal decisions of domestic life to school bond elections to the world industrial economy. One sphere where it is hardly ever observed is the prediction and modification of human nature. The hazards of monolithic sophistocratic rationalization of fundamental human policy should not be overlooked, and medicine is wisely dedicated to the welfare of individual patients one at a time. However, though lacking machinery for global oversight, we must still find ways to cope with the population explosion, environmental pollution, clinical experimentation, the allocation of scarce resources like kidneys (transplant or artificial), even a convention on when life begins and ends, which confounds discussion of abortion and euthanasia. Concern for the biological substratum of posterity, i.e., eugenics, is divided by the same cross-purposes. Nevertheless, whether or not he dares to advocate concrete action, every student of evolution must be intrigued by what is happening to his own species (what else matters?), and especially the new evolutionary theory needed to model a self-modifying system that makes imperfect plans for its own nature.

Repeated rediscovery notwithstanding, the eugenic controversy started in the infancy of genetic science. More recently, the integration of experimental genetics and biochemistry has provoked a new line of speculation about more powerful techniques than the gradual shift of gene frequencies by selective breeding for the modification of man. This article will first recapitulate a widely held skepticism about the criteria for the "good man" who is the aim of eugenic policy. The strategic impasse will not deter tactical assaults, but favors those with the most obvious, short-run payoff. I will then show how this points to an impending revision of the experimental design of human evolution, based on precedents already established in other species of animals and plants.

The debate needed to ventilate these issues has started in a few conferences: *Man and his future* (G. Wolstenholme, ed.) Ciba Foundation Symposium, 1962; *Control of human heredity and evolution* (T. M. Sonneborn, ed.) MacMillan, 1965; and *Biological aspects of social problems* (Meade & Parkes, eds.) Plenum Press, 1965, which document many other ideas and references to primary literature. I would refer especially to Dobzhansky (1962) and Harris (1964) for outlines of the philosophical and technical foundations of the discussion.

Despite every intention of generality, the outlook of this article is unavoidably culture-bound; many of my allusions pertain to academic life in the United States and might seem utterly absurd to the vast majority of the world's population, of which we are hardly an unbiased sample. The futility of discussing the patterns of human evolution without fairer representation of its actual components is the most cogent criticism of any simplicistic definition of eugenic goals.

1) Human culture has grown so rapidly that the biological evolution of the species during the last hundred generations has only begun to adjust to it. Microscopic processes of human evolution go on, but the instability of the historical milieu obscures any coherent pattern of biological adaptation since the paleolithic. Cultural cohesion tends to mute strident biological innovation, by the exclusion of deviants (whether "positive" or "negative"). But of course it generates its own biases, with many short-term fluctuations in the selective value of different genotypes and the long term-cancellation of many advantages irrelevant to civilized life.

2) Even on the time scale of the cultural revolution, we must acknowledge a singularity in the history and evolution of the planet: the emergence of scientific insight and technological power in the present era. In one lifetime, the parish has become the solar system.

3) The historical examples of the application of technology such as armaments and the population explosion are premonitions of the future. The hazards of imbalance as between technical power and social wisdom are well advertised, but technology itself is out-of-balance. For example, the technology of arms control has only recently attracted a fraction of the scientific attention devoted to its politics.

4) There has been considerable discussion of the supposed hazard to the human gene pool from the sheltering of the tacitly "unfit" by medicine or social welfare. Not so widely understood is the futility of negative-eugenic programs: most deleterious genes are represented and maintained in the population mainly by normal (conceivably sometimes supernormal?) heterozygotes. If we attack the heterozygotes as well as overtly afflicted homozygotes, almost no human being will qualify. In addition, many well-established institutions, such as the comfort of the automobile, and of heated shelters, war, and inheritance of unearned wealth or power, are equally suspect as dysgenic. It is very difficult to see how we can reconcile any aggressive negative eugenic program with humanistic aspirations for individual self-expression and the approbation of diversity. Positive eugenic programs can be defended roughly in proportion to their ineffectiveness: applied on a really effective scale they would state the same dilemmas. At present the main hazard of these proposals is the oblique even if unintended weight they may appear to give to the enforcement of negative eugenics on outcast groups.

Genetic counseling can nevertheless play an important role within the framework of personal decision and foresight for the immediate family. It can offer grave negative cautions about inbreeding and recurrence of genetic disease; it might also encourage optimists to look for compatibility or complementarity of positive attainments as a factor in mating preference. However, the public advertisement of "superior germ plasm" (sperm banks) is open to so many distortions—like most manipulations of mass taste—that its implementation would probably run very differently from its sponsors' hopes. As in adoption proceedings, the anonymity of third parties can be set aside only at great risk to the stability of family life.

5) The cultural revolution has begun its most critical impact on human evolution, having generated technical power which now feeds back to biological nature. The last decade of molecular biology has given us a mechanistic understanding of heredity, and an entry to the same for development. These are just as applicable to human nature as they are to microbial physiology. Some themes of biological engineering are already an inevitable accompaniment of scientific and medical progress over the next five to 20 years.

The sharpest challenges to our pretensions about human nature are already in view—and may be overlooked by too farsighted focussing on more sophisticated possibilities, like "chemical control of genotype". (To save repeating a phrase, let me call this genetic alchemy, or *algeny*). Algeny is diversionary, not because I doubt its eventual realization, but because the obvious difficulties provide a too convenient refuge for evading sooner anxieties. Perhaps I might point to some analogous history. Some years ago, I suggested that the genetics of somatic cells of mammals could be worked out most directly by exploiting precedented interactions of cells in fusion, coalescence of karyotypes, and segregation. This was already being brilliantly realized, but much more energy has still been spent in vain pursuit of DNA- and virus-mediated transfer of genes in mammalian cells. These algenical visions still dominate the imagination of most of my colleagues, and may of course ultimately succeed.

The realization of applied biology is, simply, medicine; a more effective slogan on which to focus an alternative to eugenics is "euphenics," whose meaning should be transparent to readers of this journal. Euphenics then means all the ameliorations of genotypic maladjustment, including liability to any disease, that could be brought about by treatment of the affected individual, more efficaciously, the earlier in his development. Disease is any deficit relative to a desired norm, and with its shots to accelerate brain growth, the next generation or two will surely have an even more dismal clinical appreciation of our intellectual capacity than we as students did for our professors.

The eventual impact of molecular biology on medicine should be self-evident. An immediate point of application follows from the clarification of immunity. It is now certain that the next few years will see the development of tissue and organ transplantation on a large scale. It would be a mistake to think of this as merely the repair of catastrophic defects in kidney or heart. Many more of us have slighter imbalance in our homeostats, muscles, teeth, stomachs or scalps, whose amenability to exchange will add up more weightily for standards of human performance. These implants will compete with their mechanical counterparts, which already prove the eminence of the trivial. The automobile is evolving into an all-purpose exoskeleton now augmented not only with locomotors but also a variety of sensors, effectors, and communicators. As it can also be equipped with auxiliary blood-pumps, gas-bubblers, and a laundry (kidney), much of the effort that goes into making these medical devices implantable may be already irrelevant to contemporary man.

Embedded in molecular biology are the crucial answers to grave and basic questions about aging, the major degenerative diseases, and cancer; and it seems an easy gamble that very consequential changes in life-span and the whole pattern of life are in the offing, provided only that the momentum of existing scientific effort is sustained. Quite apart from the glimpses of the bizarre that mechanical and transplanted organs may offer, this is a general issue of the utmost importance to the fabric of human relationships; we have hardly begun to face it.

It is already a very heavy burden on the conscience of our physicians that the ebbing of life is a gradual process; that the spontaneous beating of the heart is no longer the uncontrollable axiom of human life; indeed that many a "person" could be maintained indefinitely as an organ culture if there were any motive for it. Biological science already has a great deal to say and more questions to ask about the foundations of personality and its temporal continuity, which we have not begun to apply to the disposition of our own lives. The whole issue of self-identification needs scientific reexamination before we apply infinite effort to preserve a material body, many of whose molecules are transient anyhow. Inevitably, biological knowledge weighs many human beings with personal responsibility for decisions that were once relegated to divine Providence. In mythical terms, human nature began with the eating of the fruit of the Tree of Knowledge. Curiously, Genesis correlates this with the pain of childbirth, an insight that the growth of man's brain has gone beyond the safe and comfortable. However, the expulsion from Eden only postponed our access to the Tree of Life.

If the limit to a brain volume of 1500 ml is dictated by the proportions of the female pelvis—and obstetrics testifies how marginal the adaptation is—the simple practice of cesarean section could set us on a new evolutionary track. Very little is now known of the embryological homeostat for size and complexity of the brain. However, the few hints from early effects of some hormones, and the "NGF" regulator of the sympathetic ganglia warrant the expectation of prophylactic control of the development of the growing brain. As such techniques become available, the responsibility for their administration can no more be evaded than for sending a child to school. Unfortunately, there are bound to be serious risks on both sides of the equation.

The elaboration of euphenics is, however, not the main purpose of a discussion of human evolution, except for the one point—the added difficulties it creates for any measure of human value. If this subject were not at the heart of the eugenic controversy, it would be arrogant to insist on the discussion of it.

Reconsider how we must reevaluate the cumulative score of a human genotype regarded over a lifetime, and for its contribution to the human future. Besides present perplexities, look to future perturbations:

1) Durability. The mere extension of lifespan alters the scores. Performance must be measured over the whole term of life, not based only on youthful precocity.

2) The euthenic context. Educational opportunity and practice are changing rapidly. Consider

a) Recognition of individual diversity. Educators have begun to learn, and exercise the knowledge, that children vary widely in the details of their information-processing machinery, e.g., the relative acuity of their sensory modalities. Many "dull" children must be reclassified as over-specialized; we might well make virtue out of necessity in enabling each child to exploit his inherent skills. This can be accomplished realistically by

b) Computer-assisted teaching. The computer display is perhaps just an extension of the printed book, but we need a much more versatile adjustment of the information channels to the subtle requirements and performance of each child. This can hardly be achieved where each teacher must deal with any number of children simultaneously. In fact, the apparent value of a genotype will fluctuate according to the current status and the availability of the teaching programs and their relevance to the values of the community! Human teachers remain indispensable for developing and guiding these programs and for their insights into motivational and social sides of their students behavior. In the long run, the individuation of the euthenic environment can only accentuate the importance of genotypic variation.

c) Within the United States and in other ways throughout the world, we observe an unprecedented experiment in equality of opportunity without regard to race. The uncontrollability of environments has left no room for the scientist to embrace any conclusions whatever about the genetic basis of differences in racial performance. Community attitudes have made genes for dark skin handicaps to academic achievement, often overriding superior brains. Many other genes play on the interaction of child and community, and ultimate human performance, just as deviously. As our knowledge of, and more to the point, the community's response to, these idiosyncrasies evolves, there will be a corresponding revision of the value equation.

d) Job skills change. Neat handwriting and mental arithmetic once crucial for white collar work are now obsolete. Tolerance for assembly line tedium is following muscular power onto the wasteheap of redundant skills. Social skills, leadership, and esthetic breadth are becoming the criteria of job success in many fields as machines take over the more routine tasks, in which logical rigor may soon be encompassed.

e) Western culture and its limited population is being succeeded by a much broader world culture. Is there much point in setting eugenic standards relevant only to a small minority of the world's population even as we watch the unprecedented breakdown of intercultural barriers? The jet airplane has already had an incalculably greater effect on human population genetics than any conceivable program of calculated eugenics.

3) The world situation. The central problem for the species must bias any momentary evaluation. Until recently, this was perceived as agricultural efficiency. Hunger still haunts the earth, but we might just manage to marshal the technical resources to assuage it. The specter of the industrialized world is suddenly nuclear suicide, and this has already led to some concern as to the biological adaptation of the species most appropriate to an age dominated by nuclear power. Political institutions are likely to change course much more rapidly than any biological response. As has been pointed out repeatedly, adaptability is man's unique adaptation.

This begs the question how to anticipate future needs, how far adaptability can be generalized, and how well it can compete, in any well-defined microniche, with more rigorous specialization. To put it another way, how do we identify the most adaptable genotypes now living and what is the price, to the detriment in special skills, of this adaptability?

4) Response to euphenics. The medico-technological context of human performance is more predictable than the socio-political. We are already committed to the attempted eradication of infectious agents like malaria, tuberculosis, cholera, variola, and poliovirus. In consequence, any breakdown of public health services can be catastrophic by exposing large, imperfectly immunized populations to these parasites. If the interplay of Hemoglobin S and malaria is a useful model, genetic adaptations to a germ-free environment are taking place too; chemical pollution might replace germs as a major selective factor except that its cumulative impact on adults is less cogent than acute infanticide. The context of modern man, in fact, includes steadily increasing reliance on medicine, i.e., euphenics, from ovulation onwards. It makes as little sense to decry genetic adaptations to this as to other components of civilized life. The quality of a genotype cannot now be evaluated in terms of a hypothetical state of nature (wherein we would quickly grunt in chilly displeasure at our unfurred skins), but must match the pragmatic expectations of the milieu of the individual and his descendants. In fact selection is so slow, especially for rare genes, as to make this a theoretical issue for some time. It would be a tour-de-force to demonstrate any change in the frequency of a specific deleterious gene in a human population that could be unambiguously traced to a relaxation of natural selection against it. In comparison to the pace of medical progress, these exigencies are trivial.

As medical practice evolves so does the evaluation of health and vigor. What has happened to pancreatic diabetes is happening to phenylketonuria, and is bound to happen to many other biochemical and developmental diseases. Indeed, it would be no surprise to find compensating advantages, in certain contexts, for some of these genotypes.

The availability of transplants and prosthetics is an extension of the social process which relaxes the demands placed on a single genotype. We can imagine the systematic use of chimerism as another way of merging the best that each of a variety of genotypes can offer.

Recall that the most successful exercises in plant breeding have not established pure lines of vigorous individuals. Instead, somewhat over-specialized strains are nurtured and the latent resources of individually unpromising parents are merged in vigorous hybrid offspring. (A good farmer has learned how common sense conflicts with reality when he tries to use ears of hybrid corn as seed for another generation.)

5) Social adjustment. We are on the shakiest ground trying to sort out the genetic basis of such social diseases as crime and delinquency. In any case we have a long way to go in elucidating how nature and nurture interact in this field; e.g., what penalty the species would suffer by extirpating every gene that might in some environment contribute to crime and rebellious behavior.[1] Instability of family life, the estrangement of the generations, and the shallowness of human communication are more prevalent and cumulatively more serious diseases than violent crime, and must be given equal account in any effort to define the "good man," or in any lament of human deterioration.

Who will toss the first stone?

6) The sexual dimorphism. Most eugenic discussions have been overwhelmingly male-oriented, as is academic life. Western culture is more paradoxical than ever in its assignment of roles to women, and thereby in the design of their education and the advertised criteria of feminine success, stressed by conflicting demands for decoration and utility, dependence and initiative. The lack of useful occupation for many older women is a premonition of the leisure society where "work may become the prerogative of a chosen elite." Half the beneficiaries of eugenic design will be women. Will their creativity and happiness be augmented in a genotype that recombines XX and a set of male-oriented autosomes? Or shall we bypass the dimorphism and evolve a race where this does not matter? To shout "Vive la différence" and then ignore it is hypocrisy.

Occupational discrimination by sex has been outlawed as a byproduct of the civil rights movement in the United States, which raises nice biological questions. The sexual dimorphism is one of the most primitive of genetic differentials. Yet, in forthcoming attempts to enforce and evade the law, we shall see how thin the scientific groundwork is to answer how far the statistics of female performance in industrial society are biologically vs. socioculturally determined. In some ways this may be even harder to answer objectively than for the racial counterpart, since we are even less able to perform a meaningful experiment. What finesse it will take to design genotypes optimized for both sexes, i.e., properly rechanneled by the developmental switch with respect to the full set of desiderata, besides the primary *sex characteristics*!

7) The leisure society. This discussion has been dominated by criteria of performance at work. The whole framework may be obsolescent on the time scale of a few generations. As machines come to do almost all of the work, and this must include managerial and inventive tasks as well as clerical and manual, what are the relevant human values? Will not boredom be

[1]Professor Walter Bodmer proposes labelling this concept "the social load."

the most pernicious disease, and a zest for life without the compulsion of labor the rare essential for the species? Play rather than work will be the substratum of human activity, and the transmutation of play into cultural progress will replace the underpinning by industrial and military technology of its superstructure of basic science.

Perhaps the scientist who works for his joy in it is the most nearly preadapted for that topsy-turvy world, obviously an impeccable criterion for eugenic choice.

This leads us finally to algeny. Man is indeed on the brink of a major evolutionary perturbation, but this is not algeny, but *vegetative propagation*. (No one will be surprised that Haldane had anticipated this reasoning years ago.)

For the sake of argument, suppose we could mimic with human cells what we know in bacteria, the useful transfer of DNA extracted from one cell line to the chromosomes of another cell. Suppose we could even go one step further and sprinkle some specified changes of genotype over that DNA. What use could we make of this technology in the production as opposed to the experimental phase?

Repair genetic-metabolic disease? Indeed, if a diffusible hormone or enzyme were involved; but the same virtues are more readily available by transplantation. The advantage is consequential only if some nondiffusible product or irreversible developmental commitment (like a neuronal pattern) were involved. However, it is utterly unreasonable to anticipate the correct reprogramming of every treated cell. Then we must perform the algeny on gamete or zygote, but in so doing we face the difficulty of testing the consequences of the intervention! If the purpose is a better human being, by any standard, we would need 20 years to prove that the developmental perturbation was the intended, or in any way a desirable one. And if it were, we would face the same hazards generation after generation. The premise of this argument is that the inherent complexity of the system precludes any merely prospective experiment in algeny. It is bound to fail a large part of the time, and possibly with disastrous consequences if we slip even a single nucleotide.

To recapitulate, if the desired effect is achieved by modifying some somatic cells, the same end is available by transplanting cells already known to have these properties. In general this should be much easier than systematically changing the existing ones. If the zygote or a gamete needs to be altered, the operation is bound to have an uncertain outcome, and needs some kind of retrospective test. This ability to manipulate zygote nuclei should depend on prior capacity for nuclear transplantation and vegetative proliferation of the involved cells—both as part of the operation, and for the experimental calibration of the results.

If we have efficacious methods for testing and selecting new genotypes, do we have much need for algeny? Would not recombination and mutation give ample material for test? Perhaps for some time. But I would credit the possibility of designing a useful protein from first premises, replacing evolution by art. It would then be requisite to implant a specified nucleotide sequence into a chromosome. This would still be useless without retrospective inspection and approval of the result, e.g., in a clone of somatic cells. What to do with the mishaps needs to be answered before we can believe that these risks will be undertaken in the fabrication of humans. But, during an experimental phase, algeny may be as useful for the generation of designed genotypes, especially if they can be verified in cell culture, as other combinatorial tricks in the geneticists' repertoire.

Vegetative reproduction, once we are reminded that it is an indispensable facet of experimental technique in the microbial analogy, cannot be so readily dismissed. In fact there is ample precedent for it, and not only throughout the plant and microbial kingdoms, but in many lower animals. Monozygotic twins in man are accidental examples. Experimentally, we know of successful nuclear transplantation from diploid somatic as well as germline cells into enucleated amphibian eggs. There is nothing to suggest any particular difficulty about accomplishing this in mammals or man, though it will rightly be admired as a technical tour-de-force when it is first implemented (or will this sentence be an anachronism before it is published?) Indeed I am more puzzled by the rigor with which apogamous reproduction has been excluded from the vertebrate as compared to the plant world, where its short-run advantages are widely exercised. If the restriction is accidental from the standpoint of cell biology, nevertheless a phylum that was able to fall into this trap might be greatly impeded in its evolutionary experimentation towards creative innovation.

Vegetative or clonal reproduction has a certain interest as a investigative tool in human biology, and as an indispensable basis for any systematic algenics; but other arguments suggest that there will be little delay between demonstration and use. Clonality outweighs algeny at a much earlier stage of scientific sophistication, primarily because it answers the technical specifications of the eugenicists in a way that Mendelian breeding does not. If a superior individual (and presumably then genotype) is identified, why not copy it directly, rather than suffer all the risks of recombinational disruption, including those of sex. The same solace is accorded the carrier of genetic disease: why not be sure of an exact copy of yourself rather than risk a homozygous segregant; or at worst copy your spouse and allow some degree of biological parenthood. Parental disappointment in their recombinant offspring is rather more prevalent than overt disease. Less grandiose is the assurance of sex-control; nuclear transplantation is the one method now verified.

Indeed, horticultural practice verifies that a mix of sexual and clonal reproduction makes good sense for genetic design. Leave sexual reproduction for experimental purposes; when a suitable type is ascertained, take care to maintain it by clonal propagation. The Plant Patent Act already gives legal recognition to the process, and the rights of the developer are advertised "Asexual Reproduction Forbidden."

Clonality will be available to and have significant consequences from acts of individual decision—Medawar's piecemeal social engineering—given only community acquiescence or indifference to its practice. But here this simply allows the exercise of a minority attitude, possibly long before its implications for the whole community can be understood. Most of us pretend to abhor the narcissistic motives that would impel a clonist, but he (or she) will pass just that predisposing genotype intact to the clone. Wherever and for whatever motives close endogamy has prevailed before, clonism and clonishness will prevail.

Apogamy as a way of life in the plant world is well understood as an evolutionary cul-de-sac, often associated with hybrid luxuriance. It can be an unexcelled means of multiplying a rigidly well-adapted genotype to fill a stationary niche. So long as the environment remains static, the members of the clone might congratulate themselves that they had outwitted the genetic load; and they have indeed won a short-term advantage. In the human context, it is at least debatable whether sufficient latent variability to allow for any future contingency were preserved if the population were distributed among some millions of clones. From a strictly biological standpoint, tempered clonality could allow the best of both worlds—we would at least enjoy being able to observe the experiment of discovering whether a second Einstein would outdo the first one. How to temper the process and the accompanying social frictions is another problem.

The internal properties of the clone open up new possibilities, e.g., the free exchange of organ transplants with no concern for graft rejection. More uniquely human is the diversity of brains. How much of the difficulty of intimate communication between one human and another, despite the function of common learned language, arises from the discrepancy in their genetically determined neurological hardware? Monozygotic twins are notoriously sympathetic, easily able to interpret one another's minimal gestures and brief words; I know, however, of no objective studies of their economy of communication. For further argument, I will assume that genetic identity confers neurological similarity, and that this eases communication. This has never been systematically exploited as between twins, though it might be singularly useful in stressed occupations—say a pair of astronauts, or a deep-sea diver and his pump-tender, or a surgical team. It would be relatively more important in the discourse between generations, where an older clonont would teach his infant copy. A systematic division of intellectual labor would allow efficient communicants to have something useful to say to one another.

The burden of this argument is that the cultural process poses contradictory requirements of uniformity (for communication) and heterogeneity (for innovation). We have no idea where we stand on this scale. At least in certain areas—say soldiery—it is almost certain that clones would have a self-contained advantage, partly independent of, partly accentuated by the special characteristics of the genotype which is replicated. This introverted and potentially narrow-minded advantage of a clonish group may be the chief threat to a pluralistically dedicated species.

Even when nuclear transplantation has succeeded in the mouse, there would remain formidable restraints on the way to human application, and one might even doubt the further investment of experimental effort. However several lines are likely to become active. Animal husbandry, for prize cattle and racehorses, could not ignore the opportunity, just as it bore the brunt of the enterprises of artificial insemination and oval transplantation. The dormant storage of human germ plasm as sperm will be replaced by the freezing of somatic tissues to save potential donor nuclei. Experiments on the efficacy of human nuclear transplantation will continue on a somatic basis, and these tissue clones used progressively in chimeras. Human nuclei, and individual chromosomes and genes of the karyotype, will also be recombined with cells of other animal species—these experiments now well under way in cell culture. Before long we are bound to hear of tests of the effect of dosage of the human 21st chromosome on the development of the brain of the mouse or the gorilla. Extracorporeal gestation would merely accelerate these experiments. As bizarre as they seem, they are direct translations to man of classical work in experimental cytogenetics in Drosophila and in many plants. They need no further advance in algeny, just a small step in cell biology.

My colleagues differ widely in their reaction to the idea that anyone could conscientiously risk the crucial experiment, the first attempt to clone a man. Perhaps this will not be attempted until gestation can be monitored closely to be sure the fetus meets expectations. The mingling of individual human chromosomes with other mammals assures a gradualistic enlargement of the field and lowers the threshold of optimism or arrogance, particularly if cloning in other mammals gives incompletely predictable results.

What are the practical aims of this discussion? It might help to redirect energies now wasted on naive eugenics and to protect the community from a misapplication of genetic policy. It may sensitize students to recognize the significance of the fruition of experiments like nuclear transplantation. Most important, it may help to provoke more critical use of the lessons of history for the direction of our future. This will need a much wider participation in these concerns. It is hard enough to approach verifiable truth in experimental work; surely much wider criticism is needed for speculations whose scientific verifiability falls in inverse proportion to their human relevance. Scientists are by no means the best qualified architects of social policy, but there are two functions no one can do for them: the apprehension and interpretation of technical challenges to expose them for political action, and forethought for the balance of scientific effort that may be needed to manage such challenges. Popular trends in scientific work towards effective responses to human needs move just as slowly as other social institutions, and good work will come only from a widespread identification of scientists with these needs.

The foundations of any policy must rest on some deliberation of purpose. One test that may appeal to skeptical scientists is to ask what they admire in the trend of human history. Few will leave out the growing richness of man's inquiry about nature, about himself and his purpose. As long as we insist that this inquiry remain open, we have a pragmatic basis for a humble appreciation of the value of innumerable different approaches to life and its questions, of respect for the dignity of human life and of individuality, and we decry the arrogance that insists on an irrevocable answer to any of these questions of value. The same humility will keep open the options for human nature until their consequences to the legacy momentarily entrusted to us are fully understood. These concerns are entirely consistent with the rigorously mechanistic formulation of life which has been the systematic basis of recent progress in biological science.

Humanistic culture rests on a definition of man which we already know to be biologically vulnerable. Nevertheless the goals of our culture rest on a credo of the sanctity of human individuality. But how do we assay for *man* to demarcate him from his isolated or scrambled tissues and organs, on one side, from experimental karyotypic hybrids on another. Pragmatically, the legal privileges of humanity will remain with objects that look enough like men to grip their consciences, and whose nurture does not cost too much. Rather than superficial appearance of face or chromosomes, a more rational criterion[2] of human identity might be the potential for communication with the species, which is the foundation on which the unique glory of man is built.

Coda. Recent discussions of controlled human evolution have focussed on two techniques: selective breeding (eugenics) and genetic alchemy (algeny). The implementation will doubtless proceed even without an adequate basis of understanding of human values, not to mention vast gaps in human genetics.

Eugenics is relatively inefficacious since its reasonable aims are a necessarily slow shift in the population frequencies of favorable genes. Segregation and recombination vitiate most short-range utilities. Its proponents are therefore led to advocate not only individual attention to but the widespread adoption of its techniques, and a minority of them would seek the sanction of law to enforce the doctrine. Most geneticists would insist on a deeper knowledge of human genetics before considering statutory intrusion on personal liberties in this sphere. Meanwhile there is grave danger that the minority view will lead to a confusion of the economic and social aims of rational population policy with genocide. The defensive reaction to such a confusion could be a disastrous impediment to the adoption of family planning by just those groups whose economic and educational progress most urgently demands it.

Algeny presupposes a number of scientific advances that have yet to be perfected; and its immediate application to human biology is, probably unrealistically, discounted as purely spectulative. In this paper, I infer that the path to algeny already opens up two major diversions of human evolution: clonal reproduction and introgression of genetic material from other

[2]On further reflection I would attack any insistence on this suggestion (which I have made before) as another example of the intellectual arrogance that I decry a few sentences before—a human foible by no means egregious.

species. Indeed, the essential features of these techniques have already been demonstrated in vertebrates, namely nuclear transplantation in amphibia, and somatic hybridization of a variety of cells in culture, including human.

Paradoxically, the issue of "subhuman" hybrids may arise first, just because of the touchiness of experimentation on obviously human material. Tissue and organ cultures and transplants are already in wide experimental or therapeutic use, but there would be widespread inhibitions about risky experiments leading to an object that could be labelled as a human or parahuman infant. However, there is enormous scientific interest in organisms whose karyotype is augmented by fragments of the human chromosome set, especially as we know so little in detail of man's biological and genetic homology with other primates. This is being and will be pushed in steps as far as biology will allow, to larger and larger proportions of human genome in intact animals, and to organ combinations and chimeras with varying proportions of human, subhuman, and hybrid tissue (note actual efforts to transplant primate organs to man). The hybridization is likely to be somatic, and the elaboration of these steps to make full use of nuclear transplantation to test how well these assorted genotypes will support the full development of a zygote.

Other techniques may well be discovered as shortcuts, especially how to induce the differentiation of a competent egg from somatic tissue, bypassing meiosis. This process has no experimental foundation at present, but plenty of precedent in natural history.

These are not the most congenial subjects for friendly conversation, especially if the conversants mistake comment for advocacy. If I differ from the consensus of my colleagues it may be only in suggesting a time scale of a few years rather than decades. Indeed, we will then face two risks, (1) that our scientific position is extremely unbalanced from the standpoint of its human impact, and (2) that precedents affecting the long-term rationale of social policy will be set, not on the basis of well-debated principles, but on the accidents of the first advertised examples. The accidentals might be as capricious as the nationality, batting average, or public esteem of a clonont, the handsomeness of a parahuman progeny, the private morality of the experimenters, or public awareness that man is part of the continuum of life.

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