Pediatric Research: Substance and Process¹

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Knowledge gained from research into the diseases and abnormalities of infants and children has had an impact upon the well-being of people of all ages. By investigating the diseases that befall the young, scientists have not only saved and cured those who at an earlier time would have perished, but in the process have left a rich harvest of knowledge for physicians who minister to the larger population of adults. Improved understanding of nutrition, infection, and disease prevention through immunization, as well as mastery of the chemistry and biology of derangements of bodily fluids and salts, form bench marks in this legacy of accomplishment against which other efforts may be measured.

A century of effort has brought us to our present state of success, and although many mysteries of human biology remain a consuming challenge, we are now addressing problems whose nature differs in scope and detail from studies that marked the early years of pediatric research. We have come to accept the notion that only through the dissection of the subtle events in human development can we extend our ability to treat diseases of the young; it is from this same knowledge that we can begin to comprehend those adverse events in early life that predict the morbid consequences of the declining years and foreshadow biologic aging. Indeed, our perception of where challenges lie has in part deviated from traditional preoccupation with the abnormal and moved to a study of the normal. In no case is this more obvious than in our attempt to comprehend human behavior, and the crowning event in the next century will most certainly be an announcement of unprecedented human importance: the discovery of the molecular basis of behavior.

The ever-increasing progress in health research has, without doubt, been most remarkable in the three decades that followed World War II. The intellectual energy mobilized to meet national needs for war was abruptly transferred to peaceful pursuits, and a veritable explosion of discovery followed soon after hostilities ended.

Although we all are aware of the dangers of disregarding the lessons history teaches us, the vexations of our times seem to decry historic precedents. At times, although the need to move boldly is apparent, we remain immobile, uncertain of which course will be productive. The national research enterprise is facing serious constraints, and some observers have gone so far as to predict that research is opposed by public force which may paralyze action or even be sufficient to threaten survival. As an element of this larger cosmos, pediatric research faces both the general menace and, in addition, some threats which may be peculiar to it. Our ability to understand these forces and to analyze their origins, evaluate their intensity, and deflect them may well determine the future strength and vitality of research activities and our national commitment thereto.

It has been obvious for at least half a decade that the era of unfettered growth of the research enterprise had come to an end,

and with this change comes an uncertainty for the future which, along with other matters, causes unrest and concern. What are the causes for concern to which I refer? Let me list some of them.

1. The federal government continues to be the principal patron of biomedical research. Competition for federal patronage has become increasingly intense. The research and development dollar (the expression of federal patronage) is in the discretionary portion of the federal budget and, hence, vulnerable; in contrast, other elements in the budget can not be changed because they remain obligations fixed by statute or reflect service on the national debt. In the 1981 budget presented by the President to the Congress in January, only 5% of the budget of HHS, 10.9 billion out of 220 billion dollars, was discretionary (Fig. 1).
2. Although the total dollars for research has increased annually, it has kept pace neither with inflation nor with the increase in competition among investigators for those federal funds identified to support research. For example, we have added over 20 new medical schools and increased the pool of potential investigators by at least 50% in a matter of a little more than a dozen years. No comparable change has occurred in funding levels.
3. The cost of doing research has increased dramatically as measured in current dollars (Fig. 2). We buy food, pay rent, and hire laboratory assistance in current dollars, so that it is only in these terms that one can accurately measure cost. In 10 years, the cost of the average NIH grant award has risen nearly 100%—from \$50 to \$90 thousand—parenthetically, during the same period the number of awards increased by only 65%. The cost of the average grant to departments of pediatrics in this same period rose even more, climbing from \$40 to \$110 thousand, or 175%.
4. Measured in various ways including personal interviews, it is clear that biomedical research is no longer the same magnet for young physicians that it was even a decade ago. Documentation from NIH research training figures is somewhat obscured by introduction in the mid-1970's of a vigorous selection criterion, the payback requirement, but the trend is unmistakable (Fig. 3): a drop in the 1968–1977 interval from about 4000 to one-half that number of M.D.'s, and an increase from about 1600 to twice that number of Ph.D.'s. Although the vigor of biomedical research may be sustained by these young biochemists, physiologists, or microbiologists, the changing pattern of training suggests a substantial shortage in clinical investigators, a group that has formed a critical ingredient so vital to virtually all biomedical research. This shortage may soon threaten the vitality of our research efforts.
5. The investigator supported by federal funds is expected to provide a level of public accountability for his work which would have dismayed his counterpart only a decade ago. Like it or not (and many scientists do not), the public has demanded and been granted increased participation in decisions on distribution of research dollars, and the Congress expects to be a more equal partner in this decision-making than ever before. The world of research has become increasingly joined to the

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
HHS PORTION OF FEDERAL BUDGET

Fig. 1

AVERAGE COST PER AWARD

Fig. 2

world of politics, an outcome not unexpected as research has become increasingly dependent upon federal dollars. Although some individual scientists may continue to make research decisions based solely on scientific opportunity and judgment, total freedom to explore merely to satisfy curiosity is a luxury rather than a staple. The public has been led to expect results from the expenditure of public funds and measures these results at least in large part by personal experience—cure of disease, alleviation of disability, or increase in life span. Although the body of science is producing all three, it cannot always perform on command, and this creates a tension which discourages some investigators and may even induce some to leave research for the rewards of practice.

Concomitantly, it becomes increasingly difficult to justify the pursuit of fundamental research in language that convinces the layman who is puzzled by the scientists' vocabulary. The scientist also makes intuitive judgments, which may be difficult

to communicate not only to laymen, but sometimes even to peers. The scientist laments the passing of a time when support of basic research was an act of faith, practiced by a supportive and generous legislature.

- The requirement for institutional review of all clinical research appears to many investigators to occupy an unreasonable amount of their time. Although the emergence of an ethical imperative has, in fact, hardly slowed the pace of investigation, there is no question that the requirement for peer review of clinical protocols places new demands upon those who do research. Few have left research because of these new obligations, and, to my knowledge, none has denied the need for an ethical perspective when human beings become research subjects. Still, this embracing concern to define ethical imperatives has evoked a plea from more than one source for relief, and not a few have articulated their belief that the demands are onerous.

Fig. 3

Fig. 4

In the aggregate, these problems coalescing around clinical research could be expected, in today's climate of economic uncertainty and political flux, to raise questions about the actual survival of this critical activity. Despite these threatening problems, I suggest that the future is not really so bleak and that there is energy and vitality in the system. I reach this conclusion in part from leafing through the program of this meeting. Clearly, neither biomedical nor clinical research is moribund. In addition, the conclusion stems from an examination of the two institutions joined as partners to sustain vigorous biomedical research. I refer to our institutions of higher learning and the National Institutes of Health. Although I can offer no assessment of the internal strengths of the former, I am led to conclude from the material which follows that the needs of pediatric research are matters of considerable concern to the NIH.

Sponsorship is essential to the well-being of science, just as

patronage is the cornerstone of the arts. Each historic flowering of creativity has had its patrons, whether in Florence or Venice during the Renaissance or on the contemporary scene. The federal government has been and continues to be the foremost patron of American biomedical research; the principal vehicle for dispensing this largess has been the NIH. It therefore becomes most significant to examine the performance of this Institution and determine whether the NIH is fulfilling its patron role and as a matter of particular interest to me and to this audience, whether it is responsive to the needs of pediatric research.

The competing application for a research grant is the principal mode of entry by research investigators into the NIH support system. The award rate provides a most sensitive indicator of the annual changes in the interplay among submissions, approvals, funded projects, and the annual appropriation (Fig. 4). From year to year, the percentage of total NIH expenditures spent through

these individual investigator-initiated grants varies, but generally lies between 30 and 40%. It is perhaps coincidental, but of interest, that for each of the past 11 years almost exactly 30% of all these competing awards goes to new investigators.

In contrast to this regularity are the changing patterns of awards by Institutes to scientists in departments of pediatrics. We have two data sets obtained a decade apart, 1970 and 1980, which permit examination of this fluctuation (Fig. 5).

The data are presented as the sum of all grant awards and include indirect costs. During this decade, grants to departments of pediatrics increased in dollar value by almost 125%, (from \$23 to \$52 million) whereas the total number of awards decreased by 6%. The extreme variations among the NIH institutes is hardly unexpected; other findings, however, are perhaps less predictable.

The budget for the National Cancer Institute increased five and one-half times in this decade, but its grants to departments of pediatrics increased only three-fold. This contrasts with the NHLBI, which, while experiencing a three-fold budget increase during this same period, increased its funding to pediatrics by four and one-half times. By 1980, the NHLBI had become the second largest supporter of research in departments of pediatrics exceeded only by NICHD.

One more observation warrants attention: in 1980, 65% of all dollars and 75% of all awards to departments of pediatrics came from Institutes other than the Child Health Institute. The departments thus have a heavy stake in the financial well-being of the four Institutes (NICHD, NHLBI, NCI, and NIAMDD) that today account for 65% of grant dollars to departments of pediatrics. When viewed as the percentage of an Institute budget going to departments of pediatrics, the importance of the NIAMDD is also apparent (Fig. 6).

Turning now to a more difficult issue, did pediatric departments get a fair share of the NIH dollar? The question is not easy to answer, because the operative word is "fair," and no objective standards exist for comparison.

Data on the number of grants going to these departments are

available (Fig. 7). From 1974 through 1979, the funded competitive grants rose from 355 to 478 in number, figures representing almost 3% of all grants awarded by the NIH and an almost constant 2.5% of all dollars granted.

Perhaps one can approach the term fair through indirect means. The combined membership of the SPR and the APS, 1200, probably represents the current research community in pediatrics. The AAMC estimates that at present the full-time faculty members of all medical schools in the United States total about 35,000. If one can assure that all full-time faculty members engage in research (an assumption that is probably overly generous), then pediatric investigators represent about 3.5% of the pool and should logically command about 3.5% of the resources. Whether fair equates with equitable and whether the foregoing assumptions are valid remains either moot or debatable; nevertheless, one must be impressed with the congruence of these figures with the data on the previous slide, showing that over a 6-year period, pediatric departments received approximately 3% of both grants and dollars.

It might be claimed that we have only examined half of the picture, the bright side—that portion viewing only those investigators who succeed in obtaining awards. More critical insight might be obtained by seeking data on the rate of success by comparing the number of approved applications to the number of awards.

To address this issue, we can examine a decade of activity, Institute by Institute, during a period when the total number of awards rose steadily (Fig. 8). We observe considerable variation but steady growth. During this same period, the overall NIH success rate (Fig. 9), reported as funding of approved applications, was 45%. However, interspersed among the figures are percentages as high as 75 for the Neurology Institute in 1970 and as low as 14 for the Aging Institute in its third year of existence in 1976. The four Institutes that provide the major portion of funding to departments of pediatrics (NCI, Heart, Arthritis, and Child Health) tend to hover around the average, 45%.

Fig. 5

PERCENTAGE OF INSTITUTE BUDGET GOING TO DEPARTMENTS OF PEDIATRICS

Fig. 6

COMPETING AND NON-COMPETING AWARDS TO DEPARTMENTS OF PEDIATRICS* (1974-1979)

* Excludes contracts, training, and general research support.
Includes indirect costs.

Fig. 7

How did applications from departments of pediatrics fare? Figure 10 provides information for the period between 1974 and 1979, a time during which the number of competing research grant applications submitted by the faculty of these departments steadily rose from 270 to 370 per year. This number represents roughly three applications per department. Study section and councils approved about two-thirds of these applications, and Institute

directors made awards based upon merit and budget available. The bottom two lines in the chart compare the funding success of approved grant applications across the NIH as a whole with those submitted by departments of pediatrics. In 3 of the 6 years compared, pediatrics had a better rate of success than the group as a whole; once they were comparable, and in two years, the pediatric success rate was lower. On average, over this period of time, pediatric success was 45%; at the same time the success rate across the NIH was also 45%.

Perhaps less reassuring is the comparison between the study section approval rate for grants submitted by departments of pediatrics and grants from all sources. Here the average for pediatrics over the 6-year period was 66%, whereas that for all NIH submissions was 73%. Although these figures could be interpreted as a lack of fairness, the approval rate actually has little bearing on the ultimate level of pediatric funding. Adding a small number of grants per year to the approved package can have no effect upon the final number of funded grants because Institutes can support research only up to their budget limit. Because only 45% of approved grants were funded, approval rate does not affect the actual success rate.

The next issue then becomes the makeup of those groups performing the review. The term "study section" is generally reserved for primary review groups administered by the Division of Research Grants. There are currently about 14 scientists per study section, although this number may vary among study sections, and in the past, the number has generally been larger. The Institutes also utilize primary review groups, with aggregated memberships about 20% greater than that of the study sections.

In FY 79, the study sections examined 86% of grant applications submitted for review (18,204). Institute primary review groups assessed the other 14% of requests for funding. However, the

Fig. 8

Fig. 9

dollar value of those applications going to study sections was only 67% of the total applied for in that year. Thus, Institute primary review boards examined fewer grants but seemed to concentrate on those with higher price tags. The average grant reviewed by study section requested \$60,000 as compared to \$195,000 for the Institute review groups.

Each competitive grant must be reviewed by a primary review group (although not necessarily a study section) and recommended for funding by an Institute's National Advisory Council before it can be paid. In theory, an advisory council may approve for funding a grant disapproved by a primary review group, although in practice, this rarely occurs. An Institute Director may reject council advice and refuse to fund, but he is forbidden by law to fund a grant disapproved by council. Although the role of primary

review groups is clearly very important, only the councils have statutory authority for approval or disapproval.

We have attempted to dissect the anatomy of the grant review and approval process in an effort to identify the role of pediatricians. To do so, we used the Committee Management Information System, which contains records from 1973 to date and appointment data through 1982—enabling us to review a decade of activity (Fig. 11).

During this period, a total of 9716 appointments were made to one of the three classes of advisory bodies just mentioned: study sections, other primary review bodies, and national advisory councils. Of these appointees, 3.3% individuals claimed pediatrics as their area of expertise.

The 59 study sections administered by the Division of Research

COMPETING APPLICATIONS SUBMITTED BY
DEPARTMENTS OF PEDIATRICS

Fig. 10

APPOINTMENT BY AREA OF EXPERTISE CLAIMED BY APPOINTEE

Fig. 11

Grants have 1464 members with terms covering the period 1978-1982 (Fig. 12). Of this number, 2.4% are pediatricians; whereas the other two advisory classes (Institute primary review panels and councils) have, during this same period, 2030 members, of which 4.3% are pediatricians.

Twenty-nine percent of the study sections (a total of 17) have one or more pediatrician members, but the distribution is very uneven.

We cannot judge whether pediatric representation on advisory bodies is adequate or equitable. One apparent fact, however, is impressive: if the number of pediatricians currently engaged in research is 1200, and we assume that the NIH seeks its pediatric advisors from this group, then during the time span chosen, 129 pediatricians or 12% of all active pediatric investigators were serving in an advisory function to the NIH. Eight of 12 National Advisory Councils had one or more pediatricians actively serving,

DISTRIBUTION OF EXPERTISE IN STUDY SECTIONS - DRG

TOTAL STUDY SECTIONS = 59

Number of Study Sections	Number of Pediatricians*	
42	0	
11	1	11
5	2	10
0	3	
2	4	8
0	5	
1	6	6
59		35

STUDY SECTIONS WITH ONE OR MORE PEDIATRICIANS = 29%

* Area of expertise claimed by appointee.
Appointments with termination date after 12/31/78.

Fig. 12

with a total of 16 pediatricians in all, or 9.5% of all Council members.

To put these figures in perspective, membership in a number of professional societies were examined to determine participation in NIH advisory groups (Fig. 13). The analysis expresses the total advisors over a decade as a percentage of society membership in 1980. We find that among the groups chosen, participation by pediatricians is exceeded only by immunologists and pathologists. Obviously, other professional groups could be added to the list for comparative purposes, but to isolate from other disciplines or medical specialties that group that could be classified as "active investigators" is difficult (as for example among radiologists). Members of the disciplinary societies chosen are presumed to be investigators, an assumption similar to that made in selecting the Society for Pediatric Research and the American Pediatric Society.

This final slide attempts to address the question of equity within the concept of "fair compared to what?"

MEMBERSHIP IN SELECTED PROFESSIONAL SOCIETIES
SERVICE ON ADVISORY COMMITTEES - NIH

SOCIETY	# OF ACTIVE MEMBERS 1980	# ON NIH ADVISORY COMMITTEE*	% ON ADVISORY COMMITTEE
American Society of Microbiology	28,000	202	0.7
American Institute of Nutrition	1,544	177	11.4
American Association of Physicians			
American Society of Clinical Investigation	12,360	1,405	11.36
American Federation of Clinical Research			
American Society of Biological Chemists	4,572	842	18.4
The American Physiological Society	4,930	905	18.5
American Society for Pharmacology and Experimental Therapeutics	2,903	352	23.7
Society of Pediatric Research and American Pediatric Society	1,238	341	27.5
American Association of Pathologists	1,845	517	28.0
American Association of Immunologists	2,740	950	34.7

* Covers period 1973 to 1982.

Fig. 13

COMPARISON BETWEEN FEDERAL EXPENDITURES ON
RESEARCH AND HEALTH CARE

Fig. 14

As mentioned earlier, the R & D budget of the federal government is a discretionary item and hence volatile and vulnerable. Figure 14 compares two different elements in the federal budget, both of which lie within the discretionary segment. Appropriations for the Maternal and Child Health Service, which combines authorizations from portions of Titles V of the Social Security Act and Title XI of the Public Health Service Act, is a discretionary service budget. This budget is every bit as discretionary as the NIH budget but measures in some subtle way the federal commitment to provide services for children to whom the private sector does not make care available. This budget by no means measures the total federal outlay for children's services, of course, but is probably as good an indicator as we have available on the attitudes of Congress and the Administration toward children. It represents but a small fraction of the total expenditures on services for children of which Medicaid forms the largest component. From an operational perspective, Medicaid expenditures, however, are determined by state decisions, and the federal Medicaid administration must conform financially to decisions made outside the Congress and the administration. Thus, the MCH budget appears to offer a valid reference point for the desired comparison.

Data are available on research grants to departments of pediatrics in 1970 and 1980 and expenditures by the NIH for research related to the diseases and abnormalities occurring in the first 5 years of life in 1970. In 1970, the latter figure was almost exactly three times that of outlays to departments of pediatrics and according to the Chief, Research Analysis and Evaluation Branch, DRG, this same ratio prevails in 1980. Accordingly, I have made the assumption that these fixed points are connected by a straight line, although recognizing that like all budget graphs, the line should look more like a profile of the Himalayas than that of central Nebraska. For this comparison, however, the assumption is probably reasonably accurate.

The MCH appropriations are depicted for the same 11 years as the research expenditures and a percentage has been calculated to compare grants for research in disease of children under 5 years of age to dollars spent on MCH services. You will note that although both service and research budgets have risen substantially in the period under review, the research elements rose by 122% although appropriations for service increased by just 70%. The research side comprises an ever-increasing portion of the service expenditure. To the extent that the variables examined on this slide measure attitudes and willingness to commit resources to child issues, the research side has clearly fared better than service in the discretionary budget.

Although the data presented suffer from the need to extrapolate and in certain instances make assumptions or use proxy data when hard facts are unavailable, they do appear to present a picture of internal consistency for departments of pediatrics. The 3% figure continues to recur. Thus, the melon seems to have been cut so the slices are remarkably similar year after year. What we cannot say is whether the melon was sufficiently large to begin with. Nor can these data reflect what research needs to be done that cannot be undertaken for lack of support. Similarly, we cannot know whether some young Pasteur has been driven from the laboratory bench, never to attempt a life of scientific inquiry, because the hurdles to success appeared insurmountable.

Finally, it is not clear whether federal patronage of biomedical research is sufficiently large to meet our national responsibilities; but, then, this is a political decision and beyond our purview. Unless the number of new minds drawn to research is maintained at some critical level and the number of new starts is sufficient to

maintain current momentum, there is reason for concern. We cannot predict the future, and we recognize that the research enterprise is hostage to events over which we have no control. Although there is no justification for complacency, neither is there reason for despair.

I would now like to return to the issue of process and substance. What we have used as illustrative data falls in the domain of process. There are kinds of process other than those addressed above, embodied by organized groups or individuals seeking an audience with Congressmen, congressional staff, Departmental Secretaries, Assistant Secretaries, and now and again with the leadership group of NIH. All seek to influence the decision-making process so that resources for pediatric research will be sustained or increased. This list of power brokers is incomplete, but it does reflect the principal actors in the drama of budget formation.

While it is difficult to measure the impact of such interaction or to compare the budget in years when this consultation was intense or extensive with those in which it is not, the overall impression remaining is that the impact of this kind of process is obscure. Dollars given in grants to pediatric faculties seem, during the decade examined, to have been swept along with the vicissitudes of the larger budget of which they were a fractional part—federal support for biomedical research. It is this larger budget that needs champions. There is an imperative to maintain our entire research capacity at a level commensurate with national need.

At the outset, I included a litany of issues causing concerns to all those with responsibility for sustaining biomedical research. In most cases, there is little we can do to mitigate the impact of the alarming developments or blunt the effect of threats that now loom large but have probably always been with us to some degree.

My argument has been that we must look to the structure of our institutions rather than their formal processes if we seek stability in times of vicissitude. There is probably little we can do to modify the cadence of formal process by frontal conflict. We have, however, total control over the singular element that drives the process: the substance and quality of the research grant application. If the processes we have evaluated proceed as presently institutionalized, then we can expect them to recognize merit and imagination in grant applications. Consistent submission of grants that reflect the best in pediatric research will assure successful competition for whatever resources the federal government makes available. Recognizing that there are fads and fashions in research, just as in other human activities, and that support for targets of opportunity will command disproportionate temporary favor, we nevertheless can continue to build on an impressive foundation of success and assume the continuing productivity of laboratories in departments of pediatrics.

The role of this society assumes new prominence and importance as it becomes, to an ever more important degree, the vehicle for quality control. If we can meet the test of scrutiny and acceptance by a society that demands quality from its membership, then there is little doubt that our members can surmount the barriers which peer review presents, and compete successfully for NIH support with colleagues from other disciplines. I am not advocating a naive belief in Coueism—everything is better and better, everyday in every way. It is important to be informed and understand process, but manipulation of the process is no substitute for sound science. To think otherwise is to be misled. On the contrary, to accept the imperatives of excellence assures the future of pediatric research.