Measuring Improved Survival of Cancer Patients

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Recent statistics from the End Results Group of the National Cancer Institute have shown significant improvement in 54 percent of all incident cancer cases from 1950 to 1971. Recent comments on progress in cancer research, as reflected by prolonged survival and reduced mortality, must be put in proper perspective. This involves the accurate dissemination of the latest available data, a profound understanding of how past accomplishments have effected cancer treatment, and a clear description of the time-lag between the development of a new treatment and its ultimate reflection in general survival statistics.

Survival Trends

Data are based on the experience of cancer patients treated in more than 100 hospitals participating in the End Results Program. Included are hospitals associated with three population-based tumor registries (California Tumor Registry, Connecticut Tumor Registry, Massachusetts Cancer Registry) and six large university hospitals throughout the U.S. They represent a broad spectrum and provide a basis for assessing trends in cancer management in this country.

One-year and five-year survival trends for patients with lymphomas and leukemia are shown in Table 1. Some improvement has occurred in patients with reticulum cell sarcoma and lymphosarcoma. Additional gains can be expected, according to a recent report by DeVita and colleagues, showing actual cures using combination chemotherapy in 40 percent of patients with advanced reticulum cell sarcoma, usually considered invariably fatal and only temporarily responsive to chemotherapy. For Hodgkin's disease patients, there has also been an impressive improvement in five-year survival during the late 1960s: an increase from 31 percent in the 1950s to 52 percent during 1965-69 for men, with similar rates for women. One-year survival rates indicate continued advances in the 1970s—more than 80 percent for both men and women. These gains have occurred as a result of new treatment methods introduced in the mid-1960s. Improved survival for children with acute leukemia has also been impressive, as has survival for children with osteogenic sarcoma who are now being treated with high doses of methotrexate and citrovorum factor "rescue," administered immediately after initial surgery.

Five-year survival rates for patients with solid tumors (Table 2), representing approximately 36 percent of all
Table 1.
One-year, Five-year Relative Survival Rates
Lymphoma and Leukemia
1950–1971

| Disease               | Male 1950–1960 | Male 1960–1964 | Male 1965–1969 | Male 1970–1971 | Female 1950–1960 | Female 1960–1964 | Female 1965–1969 | Female 1970–1971 |
|-----------------------|----------------|----------------|----------------|----------------|------------------|------------------|------------------|------------------|
| Reticulum cell sarcoma| 1-year 35      | 26             | 54             | 1-year 35      | 26               | 54               | 1-year 35      | 26               |
|                       | 5-year 16      | 32             | 61             | 5-year 16      | 32               | 61               | 5-year 16      | 32               |
| Lymphosarcoma         | 1-year 54      | 26             | 54             | 1-year 54      | 26               | 54               | 1-year 54      | 26               |
|                       | 5-year 32      | 32             | 61             | 5-year 32      | 32               | 61               | 5-year 32      | 32               |
| Hodgkin's disease     | 1-year 66      | 31             | 66             | 1-year 66      | 31               | 66               | 1-year 66      | 31               |
|                       | 5-year 38      | 38             | 78             | 5-year 38      | 38               | 78               | 5-year 38      | 38               |
| Multiple myeloma      | 1-year 36      | 6              | 43             | 1-year 36      | 6                | 43               | 1-year 36      | 6                |
|                       | 5-year 12      | 12             | 16             | 5-year 12      | 12               | 16               | 5-year 12      | 12               |
| Acute leukemia (All ages) | 1-year 14      | 1             | 23             | 1-year 14      | 1                | 23               | 1-year 14      | 1                |
|                       | 5-year 26      | 32             | 40             | 5-year 26      | 32               | 40               | 5-year 26      | 32               |
| Acute leukemia (Under 15 years) | 1-year 26      | 1             | 46             | 1-year 26      | 1                | 46               | 1-year 26      | 1                |
|                       | 5-year 13      | 3             | 40             | 5-year 13      | 3                | 40               | 5-year 13      | 3                |
| Chronic leukemia      | 1-year 56      | 22             | 61             | 1-year 56      | 22               | 61               | 1-year 56      | 22               |
|                       | 5-year 56      | 25             | 69             | 5-year 56      | 25               | 69               | 5-year 56      | 25               |

*Source: End Results in Cancer, Report No. 4  tProvisional Rates

Cancers have also shown noticeable improvement since the 1950s. In addition, more than 54 percent of incident cancers have increased survival rates (Table 3.), based on comparisons of one-year survival data for cases diagnosed in 1960-64 with those diagnosed in 1970-71. Improved survival was defined as: three percentage points or more increase in survival and statistical significance at the .01 level; or, 10 percent or more improvement in possible increase in survival (e.g., if 1960 survival was 80 percent, a 20 percent increase is possible: 10 percent of 20 percent = two percentage points). The 54 percent rate is a minimum estimate, since cancers which individually make up less than one percent total incidence were not considered; combined, about 14 percent of all cancers fall into this “relatively rare” category.

Survival change can also be interpreted by the amount of person-years lost. Obviously, deaths at older ages have little effect on the loss of lifetime, compared to deaths at young ages. For example, a relatively small number of deaths early in life from leukemia result in a large loss of person-years during expected lifetime. Table 4 shows the person-years lost from the leading types of cancers in 1968. For males, improved five-year survival has occurred in
Table 2. One-year, Five-year Relative Survival Rates
Solid Tumor Sites Showing Improvement 1950–71

| Sites         | Male          | Female         |
|---------------|---------------|----------------|
|               | 1950–1959     | 1960–1964      | 1965–1969      | 1970–1971      | 1950–1959     | 1960–1964      | 1965–1969      | 1970–1971      |
| Larynx        | 78 79 84 83   | 79 79 87 84    |                |                | 56 54 62 62   | 57 52 59 59    |                |                |
| Lung          | 22 25 26 28   | 27 30 33 33    |                |                | 7 8 8 8       | 11 12 12 12    |                |                |
| Breast        | – – – –        | 87 88 89 90    |                |                | – – – –        | – – – –        |                |                |
| Prostate      | 77 81 84 85   | – – – –        |                |                | 47 52 56 56   | – – – –        |                |                |
| Testis        | 73 80 84 81   | – – – –        |                |                | 61 65 67 67   | – – – –        |                |                |
| Kidney        | 52 57 60 59   | 56 63 63 66    |                |                | 32 35 39 39   | 36 38 44 44    |                |                |
| Bladder       | 72 75 79 80   | 69 71 74 74    |                |                | 55 57 61 61   | 53 56 60 60    |                |                |
| Melanoma of skin | 77 51 52 61   | 83 60 70 73    |                |                | – – – –        | – – – –        |                |                |
| Brain         | 36 36 45 46   | 41 43 49 47    |                |                | 22 21 27 27   | 28 27 32 32    |                |                |
| Thyroid       | 76 83 86 85   | 86 87 89 88    |                |                | 70 77 78 78   | 83 86 87 87    |                |                |

seven of the 12 leading types of cancer (lung, lymphoma, leukemia, prostate, brain, bladder and kidney); for females, in five of 12 (breast, lung, leukemia, lymphoma and brain).

Do these improvements represent a "dramatic breakthrough" in cancer research and application? Some would say they are meaningless and insignificant. On the other hand, many thousands of Americans alive today would disagree. Improved survival measured by a few percentage points represents many lives saved: a four percent improvement in female breast cancer applied to 89,000 new cases annually totals 3,560 women saved each year.

Implications for the Future
The greatest improvement in survival has indeed occurred in patients with relatively rare forms of cancer, notably leu-
kemia and some types of lymphoma, particularly Hodgkin’s disease. However, knowledge gained from these successes has quickly been transferred to treatment regimens for several more common types of cancer, which were previously more resistant to treatment. Of profound significance has been a change in the conceptual approach to the treatment of cancer. In the past, the primary disease was usually treated by local eradication either with surgery alone or surgery and radiotherapy. If no residual disease was apparent, the patient was presumed to be disease free and given no further treatment. Yet, approximately 60 percent of all cancers would eventually recur (strongly suggesting that they had never been completely removed), and these were then retreated with radiotherapy and eventually chemotherapy, probably using several drugs administered sequentially. Thus, the disease was pursued, but usually never caught. With the successful treatment of childhood leukemia, involving “prophylactic” radiotherapy of the craniomeninges for sequestered leukemic cells, and of Stage IIB and IIIB Hodgkin’s disease using “prophylactic” chemotherapy, the potential beneficial effects of adjuvant therapy have emerged. Many oncologists now believe that a majority of cancer patients

| Site/Type                  | One-year Survival | Increase In Survival | Percent of Possible Improvement | Percent of All Incidence |
|----------------------------|-------------------|----------------------|--------------------------------|--------------------------|
|                            | 1960-64 | 1970-71 |                     |                          |                         |
| Breast (female)            | 88    | 90     | 2                   | 16                        | 13.9                     |
| Lung                       | 25    | 29     | 4                   | 5                         | 13.1                     |
| Prostate                   | 81    | 85     | 4                   | 21                        | 7.9                      |
| Bladder                    | 74    | 79     | 5                   | 19                        | 4.6                      |
| Pancreas                   | 10    | 14     | 4                   | 4                         | 3.1                      |
| Brain                      | 39    | 47     | 8                   | 13                        | 1.6                      |
| Melanoma of skin           | 84    | 87     | 3                   | 19                        | 1.5                      |
| Larynx                     | 79    | 83     | 4                   | 19                        | 1.4                      |
| Leukemias and Lymphomas    |        |        |                     |                           |                          |
| Chronic leukemia           | 61    | 68     | 7                   | 18                        | 1.4                      |
| Acute leukemia             | 21    | 36     | 15                  | 19                        | 1.2                      |
| Hodgkin’s disease          | 73    | 82     | 9                   | 33                        | 1.1                      |
| Multiple myeloma           | 44    | 56     | 12                  | 21                        | 1.1                      |
| Lymphosarcoma              | 60    | 67     | 7                   | 18                        | 1.0                      |
| Reticulum cell sarcoma     | 35    | 46     | 11                  | 17                        | 0.6                      |
| Childhood (< 15) Cancer    | 55    | 70     | 33                  | 53.5                      | 54.7                     |
have microscopic foci of metastatic disease and that initially combining adjuvant chemotherapy with surgery and radiotherapy holds the best opportunity for future, major successes in cancer treatment. It appears that this concept will prove useful in several forms of cancer, including some of the more common types. Adjuvant chemotherapy has already proved effective in Wilms' tumor, osteogenic sarcoma and possibly, Ewing's sarcoma. In breast cancer, the leading cause of death and years lost by women from cancer, three studies suggest that major advances are forthcoming. In colorectal cancer, the second leading cause of cancer deaths in both men and women, a recent report indicates that adjuvant combination chemotherapy holds great promise. Opportunities for applying years of research toward major improvements in treatment have never been greater or more exciting.

**From Research to Application**

There is an unavoidable time-lag between a new discovery, whether in prevention, diagnosis or treatment, and its widespread application and reflection in altered national statistics. For example, it may take a minimum of 10 years before the application of results of a clinical therapeutic trial could be expected to show a change in survival or mortality among the general population. First, the initial clinical trial is usually carried out for five years, although some are terminated sooner, as was Fisher's study of adjuvant chemotherapy in breast cancer. Secondly, favorable results of the initial study must be confirmed, usually by investigators from institutions in different geographic areas with different patient populations. This may take three to five years. Thirdly, the initial therapeutic regimen may be complicated to administer, using high doses of toxic drugs and requiring extensive technical
support, such as adjuvant methotrexate and citrovorum rescue for osteogenic sarcoma.\textsuperscript{3} In these situations, application in local and community hospitals may be technically unfeasible; patients must then be brought to the technical capabilities or the therapeutic regimen must be modified so that it can be brought to the patients. These alternatives involve extensive professional and public educational efforts and require time.

If one uses improvement in five-year survival as the end point of measurements, one must wait five years after the last patient was entered into the original three-year clinical trial—an absolute minimum of eight years after the first patient was treated. Any reflection in national statistics requires another three to four years to allow for data gathering, quality control, key punching, editing, analysis, printing and so forth.

Thus, it could reasonably be argued that the National Cancer Institute and the American Cancer Society have, in fact, done a very good job not only in therapeutic research, but also in its dissemination to the profession and its application to many Americans. Statistics through 1971 already show increases in survival for those cancers in which improved treatment became available in the mid-1960s—leukemia, lymphoma and childhood cancers. Until recently, very effective means of treating the more prevalent types of cancer were not available; now, a new era of cancer treatment is possible. For men and women, colorectal and breast cancers alone account for 188,000 of the 655,000 new cancer cases per year (29 percent). If new treatments for these and other types of cancer are discovered, confirmed, improved on and incorporated into general practice as rapidly as is scientifically feasible, even more substantial reduction in cancer mortality should be evidenced.

The National Cancer Program began with the passage of the National Cancer Act in December of 1971, which for the first time gave the National Cancer Institute a specific mandate for a Cancer Control Program.\textsuperscript{11} The Program was first fully operative in 1973. Thus five-year survival figures based on data collection ending in 1969 can in no way speak for or against the success of the Program. Its successes to date, coupled with future opportunities, provide a compelling justification for the Program, not an argument against it. By no means does this imply that efforts of the Program should not be reflected in national statistics; they should be. The whole process, however, must first be put in the proper perspective and, only then, can the Program be evaluated.

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