Ridit Analysis of the Effects of Carcinostatic Chemicals on the Growth Indices of the Nelson Mouse Ascites Tumor

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The evaluation of the effects of drugs on the growth of transplanted ascites tumors in laboratory animals can be based on the performance of different growth indices (2). Some of them (e.g., the total number of free tumor cells in the peritoneal cavity, the total packed cell volume) measure directly the increments of the tumor cell number or volume, whereas the other indices (e.g., survival time, body weight) are of an indirect nature, and their usefulness for screening purposes must first be established in an empirical way.

In a previous communication (3) the performance of several growth indices of the Nelson mouse ascites tumor growing in untreated mice and in those treated with 6-mercaptopurine has been compared and evaluated by three different statistical procedures. The technic of "ridit analysis" (1) has been found to be particularly useful when a comparison of different growth indices on the same dimensionless scale is desired. Such a technic permits making statements concerning the probability that an animal undergoing treatment A will be better off than an animal undergoing treatment B (which may be: no treatment at all = "negative control," or a treatment with some standard drug = "positive control"). An average ridit has the same interpretation (probability that a treated animal will be better off than a control animal) for all types of indices, which makes the direct comparison of ridits for different indices meaningful.

In the present publication, the technic of ridit analysis has been applied to the tumor growth inhibition data collected in the course of two series of experiments in which mice bearing the Nelson mouse ascites tumor in either fluid or solid form have been treated with a selected group of chemicals.

MATERIALS AND METHODS

ICR male mice, weighing 18–22 gm. at the time of the tumor inoculation, were given inoculations intraperitoneally or intramuscularly of 0.2 ml. of a suspension of the Nelson mouse ascites tumor cells, containing $10^6$ tumor cells in this volume. Animals were given Purina Chow pellets and water ad libitum.

In the first series of experiments, each experimental set consisted of one untreated group of mice ("negative control"), one group of mice ("positive control") treated with seven daily intraperitoneal (I.P.) injections of 15 mg/kg/day of 6-mercaptopurine (6-MP), and of seven to eight groups of mice treated with seven daily injections of different chemicals. Each group of mice consisted of twelve animals. Four mice, given injections intraperitoneally, were sacrificed on the 7th day after the tumor inoculation, and the total packed cell volume (TPCV) was determined. In the second group of three mice, given inoculations intraperitoneally, the number of survivors at the end of 20 days after tumor inoculation was recorded. In five more mice, given inoculations in the thigh muscles of the right hind leg, the tumor diameters were measured with calipers in two dimensions on living animals, and the total body weight change (carcass and tumor) was determined on the 7th and 14th days.

In the second series of experiments each experimental set consisted of one negative control group, one 6-MP-treated positive control group, and of four groups of mice treated with different chemicals. In this series each group included 22 animals. Twelve mice were allocated for the determination of the same indices as in the first series, and an additional ten mice, inoculated intraperitoneally, were observed for 6 weeks, and their median survival time was calculated.

In both series of experiments each experimental set of tests was repeated 3 times.

The growth index values obtained for each individual animal and the calculated average values were subjected to ridit analysis (1).

1 Total packed cell volume = ascites volume in a mouse X per cent of packed cell measured in a cytocrit.
RESULTS

Since this paper makes use of data which, in part, had been employed in a previous paper (3) it seems desirable to make clear the difference in the objectives of the two publications. In the first paper the purpose was to compare the performance of six growth indices which could potentially be used for cancer chemotherapy screening on ascites tumors. It was found that the TPCV showed the greatest power of discrimination between the positive and the negative control, and for this reason it was employed in the present study. The survival time has been included because of its wide use in nonsolid tumor chemotherapy screening programs (ascites tumors, leukemias). The third index, the diameter of tumors, was used because it is widely employed for solid tumor screening.

The present study has two objectives which differ from that of the previous publication. The first objective here is to assess the utility of a dual control study as an instrument for detecting active test agents. The second objective is to assess the utility of the ridit analysis with dual control for the intercomparison of a series of test agents. We will start with the results for the TPCV because they yield a clear-cut and relatively simple picture (at least in this particular study).

1. Total packed cell volume (TPCV).—In the two experimental series 38 drugs have been administered to a total of 468 mice in which the TPCV determinations have been performed. An additional 87 mice were treated with 6-mercaptopurine, and another 87 mice were used as untreated controls.

The individual TPCV values for each type of treatment in each experiment have been converted into ridits. The numerical values of TPCV and of the corresponding ridits, obtained in experiment No. 4 of the second period of the second experimental series, are presented in Table 1 as an illustration of the ridit technic.

The ridits, always having numerical values from 0 to 1, have been plotted as ordinates on a graph in which the abscissa represents the individual experiments, conducted on a group of test chemicals, and their over-all mean. In each graph the average value of the ridit for the control animal is, by definition, 0.5, and is represented by a solid horizontal line. The 95 per cent control band for the control ridit is indicated by dotted lines above and below the average control ridit line. In individual experiments the confidence interval is based on five animals in the first series, and on four animals in the second. For the total series the interval is based on fifteen and twelve animals, respectively.

The observed values for the control ridits are indicated by circles with a dot in the center for the untreated “negative” controls, and by squares with a dot for the 6-MP-treated “positive” controls. The test agents are indicated by the

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXAMPLE OF CALCULATION OF AVERAGE RIDITS, SERIES II—PERIOD 2—EXPERIMENT 4—TPCV</td>
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<table>
<thead>
<tr>
<th></th>
<th>Untreated mice</th>
<th>Aminopterin-treated mice</th>
<th>6-MP-treated mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original values</td>
<td>Ridits</td>
<td>Original values</td>
<td>Ridits</td>
</tr>
<tr>
<td>(ml.)</td>
<td>(ml.)</td>
<td>(ml.)</td>
<td>[ml.]</td>
</tr>
<tr>
<td>1.71</td>
<td>0.4606</td>
<td>1.89</td>
<td>0.2566</td>
</tr>
<tr>
<td>1.23</td>
<td>0.7829</td>
<td>0.31</td>
<td>0.9803</td>
</tr>
<tr>
<td>1.76</td>
<td>0.4014</td>
<td>0.01</td>
<td>0.9803</td>
</tr>
<tr>
<td>1.71</td>
<td>0.4606</td>
<td>1.56</td>
<td>0.5329</td>
</tr>
<tr>
<td>Sum of ridits (Σw)</td>
<td>2.1055</td>
<td>2.7501</td>
<td>3.5922</td>
</tr>
<tr>
<td>Average ridit (w)</td>
<td>0.5264</td>
<td>0.6875</td>
<td>0.8950</td>
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<table>
<thead>
<tr>
<th></th>
<th>Untreated controls</th>
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</thead>
<tbody>
<tr>
<td>1.71</td>
<td>0.0063</td>
</tr>
<tr>
<td>1.23</td>
<td>0.0063</td>
</tr>
<tr>
<td>1.76</td>
<td>0.0063</td>
</tr>
<tr>
<td>1.71</td>
<td>0.0063</td>
</tr>
<tr>
<td>Sum of ridits (Σw)</td>
<td>0.8940</td>
</tr>
<tr>
<td>Average ridit (w)</td>
<td>0.0910</td>
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<table>
<thead>
<tr>
<th></th>
<th>6-MP-treated mice</th>
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<tbody>
<tr>
<td>1.71</td>
<td>1.5658</td>
</tr>
<tr>
<td>1.23</td>
<td>1.7400</td>
</tr>
<tr>
<td>1.76</td>
<td>1.7400</td>
</tr>
<tr>
<td>1.71</td>
<td>1.7400</td>
</tr>
<tr>
<td>Sum of ridits (Σw)</td>
<td>1.7400</td>
</tr>
<tr>
<td>Average ridit (w)</td>
<td>0.4370</td>
</tr>
</tbody>
</table>

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symbols shown in Table 2. Note that due to the large number of compounds involved the same symbol has been used for different compounds in different periods.

When the experiment is in good control the control ridits should fall within the limits of the band (between the two dotted lines).

Chart 1 illustrates the ridits calculated for a group of four test chemicals and for the two types of controls (negative and positive). In this chart the data for the negative untreated controls serve as the basis of reference. One out of three control ridits falls beyond the confidence limits, indicating that not all the experiments in this series were in strict quality control. The average control ridit for the whole group of three experiments is well within the confidence limits band.

The values of TPCV ridits for the animals treated with 6-MP (individual values as well as their average) are all located above the upper confidence limit. Thus, in this experiment the TPCV index is discriminating well between the 6-MP-treated and untreated tumors.

Of the four compounds used in these experi-

### TABLE 2

**CODE OF SIGNS USED IN CHARTS 1 TO 12**

Seven daily doses, injected I.P. or S.C., starting on the day following tumor implantation.

<table>
<thead>
<tr>
<th>Sign</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Period 3</th>
<th>Period 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Daily dose (mg/kg)</td>
<td>Compound</td>
<td>Daily dose (mg/kg)</td>
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<tr>
<td>○</td>
<td>Bis-β-chloroethylmethylamine = HN₂</td>
<td>0.8</td>
<td>5-Bromouracil</td>
<td>500</td>
</tr>
<tr>
<td>●</td>
<td>Carbamic acid ethyl ester = Urethan</td>
<td>750</td>
<td>D-Glucosamine-HCl</td>
<td>1000</td>
</tr>
<tr>
<td>△</td>
<td>Colchicine</td>
<td>0.25</td>
<td>Chloramphenicol = Chloromycetin</td>
<td>500</td>
</tr>
<tr>
<td>▲</td>
<td>Potassium arsenite</td>
<td>8</td>
<td>Netropsin</td>
<td>1.25</td>
</tr>
<tr>
<td>□</td>
<td>Actidione</td>
<td>5</td>
<td>Diethylstilbestrol</td>
<td>50 subcut.</td>
</tr>
<tr>
<td>■</td>
<td>2,4,6-Trisethyleneimino-s-triazine = TEM</td>
<td>0.5</td>
<td>N-Methylacetamide</td>
<td>1500</td>
</tr>
<tr>
<td>+</td>
<td>8-Azaguanine</td>
<td>100</td>
<td>Sulfadiazine</td>
<td>250</td>
</tr>
<tr>
<td>×</td>
<td>Amethopterin</td>
<td>2</td>
<td>N,N,N',N'-Triethylthiophosphoramide = thiOEP</td>
<td>1.25</td>
</tr>
<tr>
<td>○</td>
<td>1,9-Di(methylene)sulfonyl)none</td>
<td>25</td>
<td>Urethan</td>
<td>250</td>
</tr>
<tr>
<td>●</td>
<td>N-Methylformamide</td>
<td>250</td>
<td>Aminopterin</td>
<td>0.1</td>
</tr>
<tr>
<td>△</td>
<td>0-Diazoacetyl-L-serine = Axerine</td>
<td>5</td>
<td>Amethopterin</td>
<td>1</td>
</tr>
<tr>
<td>▲</td>
<td>6-Diazo-5-oxo-L-norleucine = DON</td>
<td>0.025</td>
<td>Cortisone acetate</td>
<td>25 subcut.</td>
</tr>
</tbody>
</table>

**Series I**

**Series II**

Both series, all periods.

○ Untreated controls.

□ 6-Mercaptopurine, 15 mg/kg/day, seven daily doses.
ments two (amethopterin and cortisone acetate) have all their TPCV values lying well above the upper control limit line. The other two compounds, urethan and aminopterin, fall inside the control limits in individual experiments (4 and 6), although when the results of the three experiments are combined the TPCV ridits lie well above the upper control line. In other words, some of the individual experiments fail to demonstrate a significant difference between these two weaker agents and the untreated controls in the individual five-animal experiments. However, by replicating the five-animal studies 8 times and pooling the results (i.e., by using fifteen animals) even these weaker agents are readily detected. Although Chart 1 brings out the relationship between the test agents and the untreated controls, it is not altogether satisfactory for the intercomparison of these agents because the ridits all cluster between 0.7 and 1.0.

To be able to form a better judgment concerning the relative merits of these test chemicals, the data for 6-MP-treated controls may be used as the basis of reference. The treated control ridits are shown in Chart 2 (note that the ridit of 0.5 now represents the average ridit for the positive control group).

In this chart the untreated control values are all located at the bottom of the chart, and all the 6-MP values fall within the control limits. Both the urethan and the aminopterin values are predominantly located below the average ridit value for 6-MP, indicating that these two treatments do no better than 6-MP. Values for cortisone acetate also fall within the confidence limit band but above the average ridit for 6-MP. Only amethopterin can be regarded as doing significantly better than 6-MP, because in this case two ridits out of three—and the average ridit—lie above the upper confidence interval.

In the following Charts 3 and 4 the average ridit values for the two controls and for all the chemicals tested in both experimental series are presented (here the results for the three individual experiments have been pooled). The untreated controls constitute the reference set for the ridits in Chart 3, while the 6-MP controls are used in Chart 4.

It is evident from Chart 3 that the untreated control means are in fairly good quality control though there seems to be a downward trend.
Only in experiment No. 2 of the first series does the control ridit lie on the upper control limit line. The test agents tend to fall well above the control limits. The averages of only four compounds out of 38 (nonane, diaminobiuret, p-nitrophenyl-dimethyl-triazene, and the cinnamic acid derivative) are a little under the upper control limit line.

When the 6-MP control is used as the basis of reference (Chart 4) it is seen that:

1. All the 6-MP average values are in good quality control, since all of them are located within the 95 per cent control limits.

2. Twenty of the test agents fall below the control limits, i.e., show poorer results than 6-MP.

3. Twelve compounds are within the control limits—"borderline" drugs.

4. There are five "superior" chemicals, whose ridits fall above the control limits. They are: HN2, amethopterin (1 and 2 mg/kg/day in the first and the second series of experiments, respectively), N-methylformamide, DON, and the antibiotic actinobolin. All the "superior" chemicals are known to be effective carcinostatic agents, detected and well studied in previous screening operations on different tumor-host systems.

The performance of the ridit analysis technic in the case of the TPCV index in the present experiments can be regarded as satisfactory, although, like any other procedure, it has its limitations. Untreated control ridits (Chart 3) have been shown to be useful for the initial step in the screening. They have permitted the detection of active agents and the elimination of ineffective or slightly effective drugs.

One important distinction between ridits (as used above) and the "percentage inhibition of tumor growth" (a more familiar method of reporting results) should be noted. The "percentage inhibition" for a test agent is relative to its local control (i.e., to the untreated controls in the same experiment). However, for ridits the local control values receive no special emphasis (they represent only a small proportion of the series used as a reference class). If, however, one wishes to take the local control into account this could easily be done by working with the deviations of the test agent ridits from their local control ridits (though this will not be done here).

For the second step in the screening—the intercomparison of active compounds—the use of the positive 6-MP-control is more informative. With the help of the 6-MP ridits it is possible to classify such chemicals into those poorer than, similar to, or better than the 6-MP standard.

Here again the index of performance of the test chemicals is not affected by the behavior of the local control. The 6-MP values are rather
stable (Chart 4), and the use of an index which brings in the local control (especially the untreated control) would thereby introduce an extra source of variation without compensating benefits.

2. Diameters of solid tumors.—In this trial 38 drugs were administered to a total of 570 animals. In addition, 105 animals have been treated with 6-MP, and 105 animals were used as untreated negative controls. Once again, in order to make comparisons, the tumor diameters were transformed into ridits. On the ridit scale the smaller tumors are at the top of the scale, and the larger ones at the bottom. The 95 per cent control band has been calculated on the basis of five animals for each experiment (or fifteen animals when the three experiments are pooled).

The tumor diameter ridits for four compounds singled out for illustrative purposes in the case of TPCV are presented also in Charts 5 and 6, in which they are referred to the tumor diameter ridits for untreated and 6-MP-treated tumors, respectively.

The untreated controls in Chart 5 are not in good quality control (one value out of three is beyond the confidence limits). However, the average ridit for the untreated control is within the confidence interval, and the 6-MP average ridit of 0.78 is well above the upper confidence limit for the untreated control, indicating a good discriminatory power of this index for 6-MP. Only cortisone among the four compounds tested shows consistently high ridits.

When comparisons are made relative to the 6-MP ridits (Chart 6), the individual results obtained with cortisone appear to be no better than those obtained with 6-MP. The pooled average cortisone ridit of 0.67 is just above the upper confidence limit for the 6-MP average, indicating a slightly better performance for cortisone than for 6-MP. The remaining three compounds are less effective than 6-MP.

The average ridit data for all the 38 tested chemicals are summarized in Charts 7 and 8. It is evident from Chart 7 that the untreated control means are not in very good quality control: four untreated values out of seven lie outside the control limits. Consequently, the interpretation of these charts becomes more difficult (see "Discussion").

The comparison with 6-MP-treated control rid-
its for tumor diameter (Chart 8) shows that 6-MP controls are in somewhat better quality control: one value is above the confidence limit and one more is on the borderline.

3. Survival time.—Because survival time was included as an index only in the second series of the experiments, the number of drugs tested was sixteen (as compared with 38 for the previous indices). Survival times have been transformed to ridits, but the identified distribution consists of the second series only (120 animals). Long survival times are at the top of the ridits scale, with short survival times at the bottom.

The survival time ridits (for the four compounds previously used for illustrative purposes) are presented in Charts 9 and 10, together with the dual control ridits. Untreated control ridits are in good quality control here, but one of the treated control ridits lies on the borderline of the control chart.

In terms of the survival time, amethopterin shows the best performance, although aminopterin is also better than the untreated control. The treated ridits suggest that amethopterin is slightly superior to 6-MP, with the remaining three compounds less effective than the positive control. The average survival time ridits for all sixteen compounds tested are shown in Charts 11 and 12. From Chart 11 we see that the untreated controls are in fairly good quality control and that all the treated controls lie outside the control band (although one barely makes it). Nine of the sixteen test agents also fall outside of the untreated control band. However, from Chart 12 we see that one of the treated control points falls distinctly below the control band. In all, two of the test agents fall above the 6-MP control band, six of the agents fall inside the band or on the boundary, and eight of the agents fall below.

Unlike the situation for the TPCV and the tumor diameter, the positive control ridits for survival time appear to be less stable than the negative control ones. The reason for this behavior is that, with the TPCV and the tumor diameter, the range of the response to an active agent is constricted relative to the negative control because the scale cuts off at zero. On the other hand, with the survival time there is no such cut off for the active agent and the animals may survive for an indefinite period.

**DISCUSSION**

The material in the "Results" section has illustrated the use of a dual control combined with ridit analysis for the intercomparison of a series of test agents. While the summary graphs—Chart 3, for example—may appear rather complicated, it should be remembered that a great deal of information has been compressed into a single
Thus, Chart 3 tells the scientist much of what he needs to know to make a sensible inter-
comparison of the test agents (for example, to
select one or more of the 38 compounds for further
testing either in the laboratory or the clinic).
The inspection of the summary chart not only
informs the scientist of the performance of a
particular agent or agents which may be of in-
terest, but, in addition, it tells him quite a bit
about the performance of the screening system
that is being employed. The information about
the screen itself is really a prerequisite to an
interpretation of the results for an agent. However,
current practices in the reporting of cancer chemo-
therapy screening results often omit (or obscure)
this vital information.

When the results are presented as in Chart
3, the investigator can see at a glance whether
or not the system is in reasonably good quality
control and also whether or not the system is
doing a good job of discrimination. If the system
is in reasonably good quality control, then the
averages for the control groups should lie within
a control band 95 per cent of the time (19 times
out of 20). If the system is discriminating well,
then almost all the positive control averages should
lie well above the upper control limit (when,
as here, the convention is adopted that a higher
ridit represents a more favorable response). The
point shows quite clearly when we compare Charts
3, 7, and 11. With the TPCV and survival time
(Charts 3 and 11) the quality control is reasonably
good, whereas for the tumor diameter the negative
control averages are erratic. Hence, in interpreting
the results for a given agent the lack of reproduc-
ibility of the tumor diameter must be borne in
mind. The excellent discrimination of the TPCV
shows up clearly in Chart 3, where not only
are all the positive controls above the upper
control limit for the negative control, but, in
addition, six out of seven of the values are greater
than 0.9. If a system is losing sensitivity (i.e.,
the ability to discriminate), the investigator gets
a warning from the chart (e.g., survival time,
fourth period, second series).

When there is direct evidence that a system
is performing well (i.e., the positive and negative
control series are in reasonable quality control
and there is good discrimination) the interpreta-
tion of the charts with respect to a test agent
is very simple and straightforward. In these data...
the TPCV system performs well, so we can regard all test agents falling above the untreated upper control limit as having demonstrated some effectiveness. Similarly, there is a simple interpretation of Chart 4 (positive control ridits). The agents falling below the lower control limit are demonstrably inferior to the standard, and those falling above the upper control limit are demonstrably better than the standard. Those agents falling within the control band are not significantly different from the standard. If, in addition to this qualitative description, a numerical measure of the performance of the agent is desired, the average ridit itself will serve this purpose. The numerical value of the average ridit represents the chance that an animal given the test agent will be better off (by whatever index is being considered) than a corresponding positive control animal. For example, a ridit of 0.75 indicates that three out of four of the animals given a test agent will be better off than an animal given the standard drug. If desired, approximate confidence intervals are available for this estimate (1).

When there is direct evidence that the system is not performing well, interpretation of the charts necessarily becomes more complicated. In general, it will depend upon the particular way in which this system is misbehaving. In Chart 7, for the tumor diameter, there seems to be a more or less systematic increase in tumor diameter with time (at least for the untreated control). We might hope that such a systematic effect would show up both in the positive and in the negative controls so that some quantity (such as a difference or a ratio) would remain fairly constant in spite of the change in the system. However, we will not necessarily find any such stable quantity (indeed, this can only be determined by an empirical trial). It may be noted from the Charts 7 and 8 that, at least on the ridit scale, the differences between the positive and the negative controls are no more stable than the original averages (and the same is true for the ratio). If the differences had been stabilized, then it would be possible to base the control chart on the differences and in this way get back to the simplest situation found with the TPCV. In this event, the procedure would be analogous to those based on the principles of local control (e.g., the usual "t" test).

![Chart 11](chart11.png)
*Chart 11.—Survival time. Summary of all experiments. Reference set: untreated controls.*

![Chart 12](chart12.png)
*Chart 12.—Survival time. Summary of all experiments. Reference set: 6-MP controls.*
When the departure from quality control cannot be rectified by what amounts to a change of index (as in the tumor diameter data) there may be some other possibilities available. For example, in the tumor diameter (Chart 8) the treated control appears to be somewhat more stable than the untreated. Thus, only in the second period of the first series is the treated control badly out of line (the third period of the second series is slightly out of bounds). Apart from these periods we can make inferences concerning those agents which are distinctly better (or worse) than the positive control. However, because of the poor performance of the system we would have less confidence in our inferences. When the results are extremely erratic (as in the second period of the first series) it would seem more appropriate to repeat the experiment than to try to derive conclusions from the dubious data. It will be noted that when a system is out of control we have to take into consideration the state of affairs of the system at the time when the test agent is being run in the interpretation of the results for that agent. The ridit chart using dual control enables us to do just this.

The preceding discussion indicates how the two methodological procedures used in this paper (dual control and ridit analysis) can assist the screener to assess the relative merits of test agents. The main disadvantage of the dual control is that it utilizes animals which could otherwise be used for screening agents. For example, in the experiments reported here the plan often called for four test agents and a dual control. By substituting another test agent for the positive control, screening production could have been increased by ~5 per cent. The question, then, is: In what situations do the advantages of a dual control more than offset this loss in production?

The use of the dual control can be regarded as a modification of screening technique in the direction of the conventional bioassay. In a bioassay the relative potency of an agent is generally assessed against a standard (i.e., positive control) rather than against a null agent (i.e., negative control). In cancer chemotherapy screening the departure from the usual bioassay approach was necessary because there were no standard agents. In the past (and in present-day primary screens) the investigator wishes to pick up agents with any sign of chemotherapeutic activity. However, nowadays quite a number of active agents (in animal systems) are known, and the emphasis is shifting to the detection of agents which are at least as potent as those already known. For this purpose the dual control is most useful, and its advantages are likely to outweigh the loss in production.

**SUMMARY**

1. Effects of 38 carcinostatic test chemicals on the total packed cell volume, tumor diameter, and survival time indices of tumor growth have been studied in mice bearing the Nelson mouse tumor in ascites or solid form.
2. The usefulness of a system of dual controls in each experiment, including a negative untreated control and a positive control treated with a standard drug, has been illustrated.
3. The results have been evaluated by means of ridit analysis, facilitating the intercomparison of a series of test agents.
4. Summary charts in which the test compound ridits are compared with the untreated control ridits inform the investigator whether or not the system is in good quality control and is sufficiently sensitive. The value of such charts in the selection of agents with any sign of carcinostatic activity has been demonstrated.
5. Summary charts in which the test compound ridits are compared with the standard ridits (in this paper with those for 6-MP) indicate whether a test agent is inferior, equal, or superior to the standard drug. Such charts also provide the numerical measure of the performance of the index for individual test chemicals.
6. Of the three indices studied, the total packed cell volume has shown the best performance in terms of its capacity to detect active chemicals and to eliminate the ineffective or slightly effective ones.
7. The tumor diameter did not perform well, since both the untreated and the 6-mercaptopurine (6-MP) ridits were not in good quality control, the untreated controls being less stable than the 6-MP-treated ones.
8. The survival time index was of an intermediate value between those of the total packed cell volume and of tumor diameter. The 6-MP-treated ridits were less stable than those for untreated controls, owing to the capacity of the successfully treated animals to survive for an indefinite period of time.

**REFERENCES**

Ridit Analysis of the Effects of Carcinostatic Chemicals on the Growth Indices of the Nelson Mouse Ascites Tumor

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