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Organization and Remarks of Blind Screening

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Commentary

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Commentary

The screening of drugs involves scanning and evaluation. The scanning always involves a test or a group of tests which, it is believed, will permit the detection of physiological activity [1]. Unless the test is unusually rigorous the scanning must be followed by an evaluation, through another test. So, that the uncertainty of the scanning is removed. Thus some of tests to be described in this chapter are scanning methods, generally designed to permit rapid detection of activity, whereas other tests are quite specific for the evaluation of a substance and would be used only when some activity of a certain kind had been shown, at least crudely, in the scanning procedure. Still other tests are of a type intermediate to these, that is, they permit scanning with sufficient refinement so that a certain activity is detected when it is present, and its degree is also estimated [2].

Mainly screening is categorized into three named Simple screening, Blind screening and Programmed screening. In simple screening when one or two tests are used to find substances having a particular property, the screening is simple [3]; there is no need for battery of tests in which the interpretation of results of one test may depend on those of another test. In blind screening, if a new series of chemical substances available [4], either through isolation from a natural source or through synthesis, there may be no information on its pharmacological activity. Then blind screening ought to provide clues to potential activity, at least, and preferably, to indicate fields of activity, if they exist. In addition, the blind screening ought to show pharmacological inertness if it exists [5]. The chief purposes of the screening are to demonstrate whether the new group of substances is worthy of further attention, and to indicate which among them have the most interesting pharmacological properties [6].

Blind screening, the technique for detecting pharmacological activity in a group of substances without pharmacological history, requires considerable planning and skillful execution of the tests [7], in order to be economical of time and money [8]. The strategy of few tests, having simple procedures, to be applied to cheap animals, requires a knowledge of the tests that are known, as well as ingenuity in their combination.

In case of programmed screening, When a new drug of is sought, or when a series of compounds is to be investigated for some pharmacological effects [9] (for example, effects on the heart), a program of testing is required is provide information on the compounds that only a battery of tests can be provide [10]. The aim of the screening is more limited than for blind screening, and greater precision in the results is often expected.

In blind testing, some orientation is sought. By contrast in programmed testing, the screening has aspects beyond orientation [11]. The program may include the use of quantitative assay for immediate study of the most interesting compounds found through a similar semi quantitative assay [12], or for comparison with drugs recognized to be quite active representatives of other pharmacological class [13]. The program should provide also indications of potential side effects, and it should lead readily into a project for investigating the detailed pharmacology of the most promising substances.

Remarks of Blind Screening

Blind screening requires the discussion the best approach is one where no assumptions are made about what the probable actions of a compound may be, except when an already carefully studied series of compounds having similar structures has been investigated [14].

In order to decide quickly whether a substance is worthy of further study it is best to proceed from the general observation to other peculiar, and from exhaustive observational techniques to the use of instruments [15]. Many pharmacologists have failed to recognize the importance of observing the animal's gross behavior as a quantitative method. Despite the prejudice against subjective reporting in scientific observation, a standardized, carefully defined procedure may provide data of as much reliability and reproducibility as some objective methods [16]. The observation discrete measures should be made, such as the alertness and muscle tone of the animal [17]. These aspects are difficult to quantify and to define, and it is consequently necessary to use some device such as a set of standard observations in order to lend system to them [18].

Because individual laboratory workers differ considerably in their ability to grade different levels of an animal response it is necessary that in this kind of subjective observation the worker or a team of two workers should perform all of the work on a series of compounds [19]. One of the difficulties is that as the skill of the workers increases, there is a tendency to work faster so that the test on each animal occupies less time than it had occupied earlier [20].

More ever as the worker or team gains reality, the evaluation may be change elegantly. Of course, the procedure and the grading should depend as little as possible on skill and experience [21]. These conditions are best satisfied where the animal's behavior may be described in terms either of its frequency or of the duration in its occurrence. For example, in testing for antihistaminic activity, the number of doses of histamine until death or withstanding of repeated exposure to a histamine aerosol might be recorded. When intensity is to be measured, the observed behavior is best appraised on an all-or-nothing scale [22, 23].

In drug evolution it is important to note the whole range of quantitative changes produced by a drug and the quantitative relation between them [24]. It is unlikely that a drug can be probably evaluated until most of the major tests have been performed under conditions that are similar, in a single animal species, and by the route of administration intended to be used clinically [25]. Such uniformity in testing greatly simplifies the problem of integrating and subsequently interpreting the data.

More often one finds a tendency to confuse matters by extending the range of variables-by mixing up us many different species [26], preparations, conditions, and routs of administration as possible in investigating the different actions of a drug. In this way, an enormous mass of data accumulated which is almost impossible to integrate. The value of obtaining multiple data from the same species, preferably from the same animals, cannot be overemphasized.

It is here that multi-dimensional procedures are of particular value, for they permit the investigator to obtain a wide range of data from each animal simultaneously and in integrated form. From such data the dose response relations for different drug actions can be more meaningfully compared, and then be extrapolated their appearance in man [27].

All-or-none approach in measurement greatly simplifies the process of data accumulation and usually facilitates analysis- especially when one is dealing with graded measures such as ataxia or muscle weakness, which are difficult to quantify reliably [28]. This approach is particularly useful in studying relative potency or in demonstrating the occurrence of a statistically significant change. In estimating the potency and possible use of a drug, however, quantal data can be grossly misleading, and a poor substitute for graded, quantitative information. This holds especially when extreme changes have been produced through large doses [29].

Such quantal data place the investigator in the uncomfortable position of having to predict the effective dose, therapeutic ratio, or side effects of a drug in man from almost irrelevant information [30]. In drug screening a quantal approach imposes the additional danger that the investigator may overlook potentially useful and safer drugs which may be unable to produce the marked changes required by the procedure being used.

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