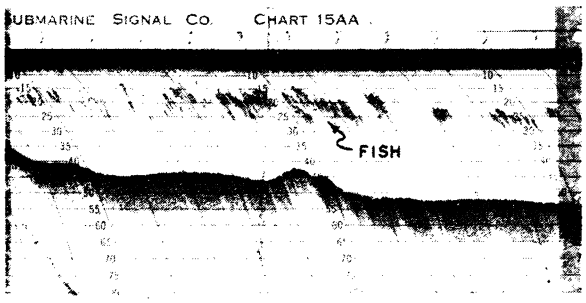

FIG. 2. Echogram of school of fish, 15–25 ft below surface.

found no schools of perch; instead, the fish had dispersed along the bottom. Individual perch were observed resting with their pectoral fins touching the sand. When disturbed by the light or the currents from the moving diver, they would move briskly ahead to escape the spotlight beam and sink again to the bottom. At daybreak they rose from the bottom, congregated in schools, and moved out to deeper water.

On a bank off Burrows Park, perch feed and hover over the bottom (depth 35 ft) at 15- to 25-ft levels during daylight hours. However, the perch schools break up and settle to the bottom by darkness. They do not move inshore as do those at Second Point. The rate of settling observed appears well within the 30% change in pressure to which a physoclist fish, such as perch, can adapt (*5*), over a 2–3-hr period.

Previously, we had assumed, on the basis of sporadic gillnet sets, that in daytime perch hovered as deep as 45 ft in summer. Our midday echograms record the great majority at 25–35 ft (Fig. 2). Therefore, the movement toward shore requires very little change in depth—chiefly a horizontal movement with only minor vertical changes. Midday echo-sounder records during July revealed heavy concentrations of fish in the areas off Second Point.

Among aquarists, a "sleep" of fishes is commonly observed. This fact was reported as early as 1874 (*6, 7*). Also, perch have been observed on the bottom of an aquarium at night (*8*).

TABLE 1

RELATIVE INTENSITIES OF LIGHT, IN FOOT-CANDLES,* AT VARIOUS TIMES AND DEPTHS FOR LAKE MENDOTA ON A TYPICAL JULY DAY

Depth, meters	Hours Before Sunset			
	3	2	1	0
Surface†	2600	2200	1000	100
2	550	460	210	21
4	168	141	64	6
6	50	42	19	1.9
8	15	12	5.7	0.67
10	4	3	1.7	0.17

* To convert foot-candles into lux, or lumens per square meter, multiply values in table by 10.

† Data for surface intensities are based on Madison Weather Bureau records for a typical clear July day; underwater intensities measured with a Weston Photronic Cell.

During summer and early fall, a rapidly changing light intensity obviously sets off the movement, but how it operates and how the fish off Second Point appear to orient toward the southern shallows rather than toward the shore in another direction remains unexplained. Light values are given in Table 1 for various depths in Lake Mendota for a typical clear July day during the migration hours.

It might be postulated that with approaching twilight the perch, accustomed to seeing one another, lose their tendency to school, settle to the bottom, and maintain contact with the sand. Also, it is possible that this nocturnal quiescent behavior could have survival value in escaping natural enemies, many of whom, like the northern pike, hunt for food at night and perceive prey principally by vibrations resulting from the latter's swimming movements. During the day the perch move to open water, an area in Lake Mendota where there is an abundant supply of plankton, their chief food, and where there are few predators.

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A Method for Quantifying the Intensity of Pain[1]

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With the development of pharmacology as it applies to the influence of drugs on sensation, there is a need for demonstrating whether one can in fact deal with the matter of intensity of subjective responses and the modification of intensity by chemical agents. Two aspects of this problem will be dealt with: First, a means for indicating and following the intensity of pain in a group of individuals will be presented. This is an index which permits mathematical validation of difference. Second, the use of the method in comparing the effectiveness of two analgesic agents in the treatment of severe pain will be described. Where agent A and agent B both relieve pain of moderate degree equally well, there is still the highly practical problem of determining if one is more effective than the other in relieving severe pain.

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TABLE 1

MORPHINE

No. of doses in sequence	1		2		3		4		5		6	
Response	+	−	+	−	+	−	+	−	+	−	+	−
Patients	43	38	38	25	58	15	53	15	59	22	33	7
Relieved	53%		60%		79%		78%		73%		83%	

TABLE 2

MORPHINE

Doses	1		2		3	
Response	+	−	+	−	+	−
Patients	34	11	39	9	43	7
Relieved*	76%		81%		86%	
Patients	32	8	46	6		
Relieved†	80%		88%			

* Pain did not return after 3 doses.
† Pain did not return after 2 doses.

. Measurement of pain depends upon how much analgesic is required to relieve the pain (*1–3*). To be sure this is indirect, but no more so than determination of the acidity of a solution by the quantity of standard alkali used to neutralize it. We depend upon average pain, defined as the average response elicited from 25 or more individuals in pain (postoperative), surrounded with the restrictions and controls mentioned in other papers (*1–3*). If the maximum useful dose of morphine falls far short of relieving this pain, then it seems reasonable to say that this pain has greater severity, greater intensity, than a pain that is more completely relieved by the same initial dose of the same analgesic. The concept of group effect will perhaps always be necessary in dealing with general problems of pain and other subjective ailments.

The data in Tables 1 and 2 represent the response to 10 mg morphine (salt)/70 kg body weight in patients having steady, severe pain in a surgical incision. The material was gathered as descibed earlier (*3*). In the tables and figure, pain A was 53% relieved, pain B, 76%, and pain C, 80% relieved by the same first dose of morphine. The conclusion appears to be justified that the pain that was hard to relieve and required the most narcotic before its cure was effected was the most severe, most intense pain (53% compared with 80%). Since we are dealing with a system of relativities, we require a situation where the pain is changing in intensity in a known direction, in this case toward disappearance, over a fairly well-defined time interval.

To fulfill our first task, we can construct from the data an index which represents the intensity of the pain under study:

$$\text{Average pain index} = \frac{\text{First dose effectiveness } (N)}{\text{Third dose effectiveness } (D)}$$

where the third dose represents the maximum average effectiveness of the agent. In the present instance $I = 53/79 = 0.67$. Or, in the case of the second task, to compare 2 agents, one can say

$$I = \frac{N_1/D_1}{N_2/D_2} D_1 \text{ must} = D_2, \text{ then } I = N_1/N_2.$$

If we do not impose this condition ($D_1 = D_2$) we run into absurdities that destroy the usefulness of the method. We are limiting our consideration here to 2 agents which we know (or can determine) have the same average maximum effectiveness (their curves of effectiveness approach the same asymptote), but which we want to examine to see if one is more effective than the other in relieving severe pain.

Lest there be any confusion, it must be made clear that with the same drug and the same dose, the percentage relief of pain parallels severity, intensity, of the pain. With 2 drugs in the same group of randomized patients, we have a different purpose; here, differential percentage relief permits comparison of the relative effectiveness of the 2 drugs. We cannot determine severity, intensity, of pain by comparison of 2 drugs in one group on one occasion.

To the extent that the first to third dose ratio is below unity we have evidence that the initial pain was severe. As the index approaches unity, provided the denominator represents the maximum effectiveness of the given narcotic agent, the pain is diminishing in severity. If the current effectiveness, the index, falls, the severity is increasing. One could also deal with this problem by difference of N_1 and N_2, when D_1 equals D_2. Such an approach has the advantage that statistical validation of difference is then somewhat easier than it is when the ratios are used. We prefer, however, since we are dealing in this aspect of the problem with comparisons, to think in terms of percentage gain rather than absolute gain.

When the method is used for comparison of the effectiveness of 2 agents on the severity of pain this is done in the same group of patients, half of whom are treated with one agent on the first dose and half with the other, each half of the patients on the second dose receives the agent not used on the first dose.

It can be argued when 2 agents are appraised, that one need only compare their percentages of effective-

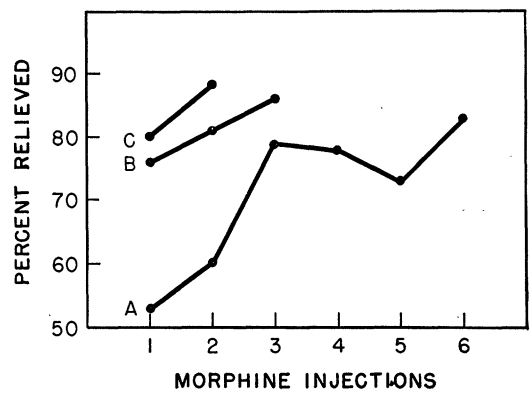

FIG. 1.

ness. This can lead to an unreal situation by implying that the possible scale is percentagewise 1–100, yet, actually, the possible range is more nearly 30–80 (from the effectiveness of a placebo to the maximum effectiveness of morphine). Use of the ratio of first and third doses, where the third falls on a line near the asymptote, thus ties the situation down to the possible.

Heretofore we have always worked with average pain. In the present study this has been broken down for the first time into 2 distinct degrees: (1) See curve A of the Fig. 1. Reasons have been presented why this represents, initially (first dose level), severe pain; (2) Curves B and C (not different from each other, but different from curve A) represent pain more completely relieved by the 1st dose of morphine. A system has been presented for indicating and following the intensity of pain in a group of individuals. This has been expressed as an index that permits mathematical validation of difference from one interval to another. Finally, a system has been described for comparing the effectiveness of 2 analgesic agents on really severe pain, agents which are undifferentiable when studied with average pain.

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Methods of Obtaining Quinones from Flour Beetles

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Flour beetles *Tribolium confusum* J. du V. and *Tribolium castaneum* (Herbst) (*1*) secrete from thoracic and abdominal glands derivatives of *p*-benzoquinone (*2*). Because these quinones occur naturally and since similar synthetic quinones have profound biological effects (*3*), investigations into the chemical and biological significance of the beetle secretion have been under way for a number of years. To obtain an ample supply of test substance we have improved existing methods (*4*) of culturing and extracting the insects.

Culturing. Eight ounces of finely ground Wheatsworth graham flour with 5% Fleischmann's pure dry yeast added were introduced with 2000 insects in a quart Mason jar. The jar was sealed by a soft rubber gasket, a screen wire circle (40 mesh), and the outer part of the screw cap. About 40 jars each were stacked in iron trays 38 in. long, 9 in. wide, and 3 in. deep. The cultures were kept in a conditioned dark room at 32° C and 80% RH. After 6 weeks, the contents of 4 jars each were sifted through a 22-mesh plastic cloth screen. The portion remaining on the sieve comprising beetles, larvae, pupae, shed skins, and other coarse material was transferred to a clean Mason jar that was sealed as before except that a half-circle of cardboard covering the lower half of the jar opening was used in place of the wire screen. The surface of the cardboard was glossy outside and dull inside the jar. These jars were laid on the beetle separator (Fig. 1) which consisted of a support, a polished steel funnel, and a beetle receiver. The insects climb up the cardboard and fall through the funnel into the receiver. An extremely clean batch of beetles is obtained in a few hours' time without further attention.

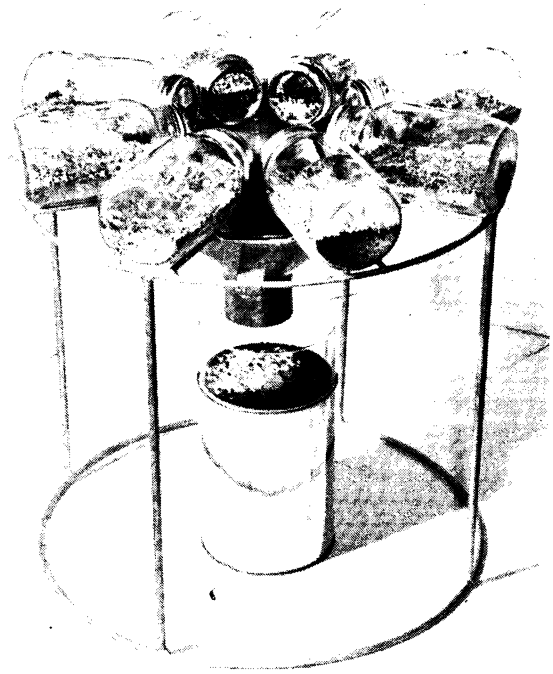

FIG. 1. Beetle separator.

In a widely used method of culturing, the jars are sealed by cloth sheeting and placed upright. We have found that our procedure yields a greater number of insects. From 10 conventional cultures each started with 2000 insects and maintained in the described environment for 6 weeks a little over 1000 additional beetles were obtained in the average per culture. With our present method, 10 jars produced in the average more than 3000 additional insects per culture. This is due, possibly, to better ventilation in the jars.

When beetles were collected for extraction, the receiver was exchanged for a cylindrical metal flask fitting the bottom of the funnel. The flask contained some dry ice and was kept surrounded by dry ice-alcohol in a Dewar flask. In this manner, the insects falling through the funnel were instantaneously anesthetized by the CO_2 atmosphere in the flask and killed by deep freezing. The quinones were thus pre-

[1] Thanks are due Louis M. Roth for his active interest in the development of the extraction method and for furnishing us with cultures of *T. confusum* and *T. castaneum*.