

sinic acid overflows into a normally minor pathway to hypoxanthine.

The administration of the xanthine-oxidase inhibitor, allopurinol [4-hydroxypyrazolo(3,4-d)pyrimidine or Zyloprim] (6), reduced the excretion rate of uric acid. In C.W. (Table 1), the amount of reduction was directly related to the dose of allopurinol. Coincidentally, the amounts of urinary hypoxanthine and xanthine increased. The excretion of xanthine increased more than that of hypoxanthine, reducing the ratio of hypoxanthine to xanthine at times to less than one. This presumably reflects the accumulation of metabolites in the inosinic acid-hypoxanthine pathway, with a diversion of inosinic acid towards xanthylic acid and xanthine.

Another significant observation is that the total excretion of oxypurines—uric acid, hypoxanthine, and xanthine—remains unchanged in patients with congenital hyperuricosuria even when they received large doses of allopurinol. This is similar to the observation reported in one case of hyperuricosuria (2) but different from the response of patients with neoplastic disease where there is rapid turnover of nucleic acids (7) and different from the response in primary nontophaceous gout (8). In both of these conditions, the increased excretion of hypoxanthine and xanthine does not compensate for the reduction in uric acid, so that the total oxypurine excretion is reduced by over 20 to 30 percent (Table 1). It has been suggested that this results from the reutilization of hypoxanthine and xanthine for nucleic acid synthesis, and new purine synthesis is reduced as the result of "feedback" inhibition of 5-phosphoribosylpyrophosphate amidotransferase by the natural ribonucleotides (9).

A lack of regulatory control has long been considered the cause of increased uric acid excretion in gout and has also been suggested, though without evidence, as the fundamental defect in congenital hyperuricosuria. Our observations are consistent with, though not limited to, the interpretation that the regulatory mechanism is at least partially effective in gout, and is ineffective in hyperuricosuria with central nervous system dysfunction. Urinary excretion accounts for only 60 percent of the synthesized uric acid (1), so that care must be exercised in interpreting the urinary values alone.

Since our manuscript was submitted, it has been reported that these children are deficient in the enzyme hypoxanthine-guanine phosphoribosyltransferase, which is responsible for the conversion of hypoxanthine to inosinic acid (10). The increased urinary excretion of hypoxanthine may now be attributed to failure to re-utilize this metabolite. The loss of regulatory control of purine synthesis suggested by our data has thus been specifically delineated. Nyhan and Sweetman have made similar observations on urinary oxypurines in four patients with congenital hyperuricosuria.

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12. We thank Dr. J. Hammond of the Willowbrook State School, Dr. M. Brust, and Dr. L. Greenspan for cooperation in the study of their patients. Support from the American Cancer Society (P330), PHS (CA 08748), and the National Foundation. The studies were done in the Special Clinical Unit of New York University Medical Center.

12 April 1967

Alarm, Defense, and Construction Behavior Relationships in Termites (Isoptera)

Abstract. Evidence indicates that building behavior in termites is a direct consequence of low-level alarm stimuli and that its immediate function is defense. As in other forms of termite defense behavior, recruitment of nymphs and workers is accomplished by trail laying in conjunction with transmission of the alarm. The number recruited is related to the intensity of the input stimulus. Primary construction ceases when the original causal stimulus is eliminated by the effects of the actual building.

The behavior of termites involved in building and in construction of nests has intrigued many workers over the years (1) and has been investigated principally by Grassé (2), and more recently by Howse (3). Grassé, on the basis of his observations of *Bellicositermes* and *Cubitermes* in Africa, has put forward a hypothesis to explain the social coordination involved in the building of a complicated termite nest. Briefly, his hypothesis of "stigmergy" is that building behavior is at first uncoordinated ("La phase d'incoordination"); when the construction at any one point reaches a certain critical density it attracts other termites topochemically. These focuses of the building material determine where the new pellets of earth used in the building are to be deposited. The constructions built thus act as new determinant stimuli for further construction. This hypothesis has not been universally accepted for a number of reasons (4). One drawback to the hypothesis

which seems to have been overlooked, or at least not to have been emphasized, is that no adequate stimulus to stop a certain piece of construction has been shown to operate. My work supports some of the hypothesis of stigmergy, but it shows that the important initial phase is not haphazard, that it involves distinct directional cues, and that a feedback mechanism to halt building is present.

Howse (3) in his very recent work on construction behavior in *Zootermopsis angusticollis* (Hagen) and *Zootermopsis nevadensis* (Hagen) does not comment on the stigmergy hypothesis. He considers air movement to be the prime stimulus in nest building activity and feels it is this movement that attracts termites to minute openings made in their nest experimentally or naturally. He suggests that the tropical termites build around air currents that are set up in a developing nest, and he rejects the suggestion (5, 6) that a sharp gradient in humidity or odor

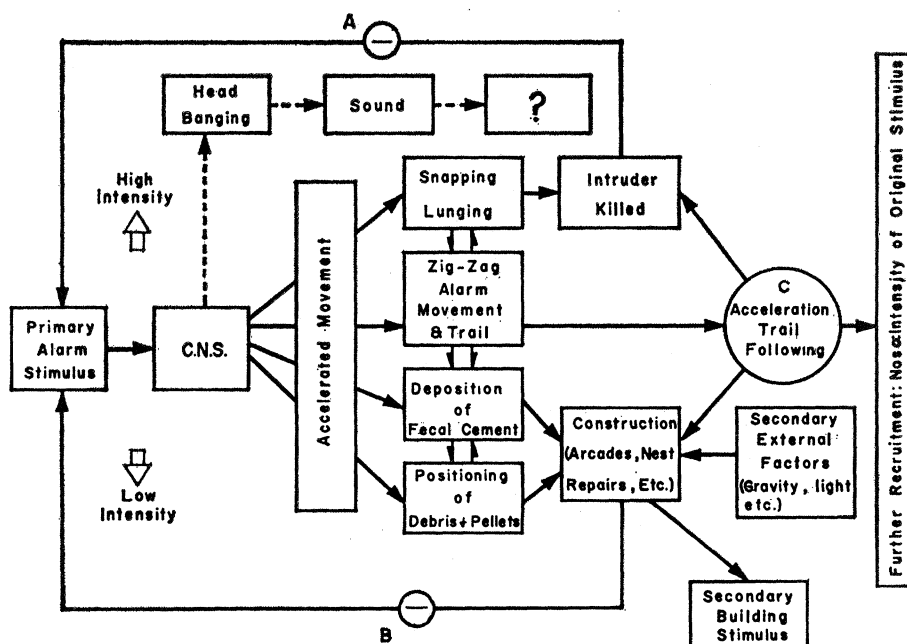


Fig. 1. Diagram of some of the reactions of termites to alarm, showing two feedback mechanisms involved in homeostasis. Probable relationship of "head-banging" behavior indicated by broken lines. A and B are negative feedback pathways. C represents a second termite.

can act as a stimulus for building. His experiments, however, can be interpreted in other ways, as will be shown, and the results of my study do not support the idea that building is only a response to air movement.

Emerson and others (1) have pointed out many times that the nests and covered runways of various species of termites have evolved as a protective device of the colony against predators and such external factors as dessication. It now appears that the building of a nest may actually have its origin in a quite immediate response to danger and that it involves at least two of the many responses of an alarmed termite.

Building behavior was observed in three species of termites, *Nasutitermes corniger* (Motschulsky) from Panama and *Zootermopsis angusticollis* (Hagen) and *Z. nevadensis* (Hagen), the two species of Californian damp-wood termites. The first species builds complex arboreal nests of carton (malaxated wood, debris, fecal pellets, and rectal fluid), while the primitive *Zootermopsis* builds walls of similar material that seal off galleries and holes in the logs that it inhabits. Despite the great difference in the end product of construction, the general methods of construction of the two genera are remarkably similar. In *Zootermopsis*, an actively building 12-mm nymph typically gath-

ers a dry fecal pellet in its mandibles and moves forward to the site where the pellet will be deposited. It then turns completely around and places a spot of liquid feces (fecal cement) on the site, turns once more, and with a characteristic side-to-side motion of the head places the pellet on the fecal cement. It then gathers another pellet and, if the fecal cement is still wet, will place the pellet directly on the fecal cement without adding any more cement. The behavior of the workers of *Nasutitermes* is quite similar, and the observations on this genus bear out the classical observations of Beaumont (7) on Panamanian nasutes. In both genera the immediate end result of this behavior is that pieces of debris or pellets are held together by the fecal cement. It is in this behavior that Grassé indicates that there is no coordination between individuals in the early stages. The stimuli which initiate this behavior were studied in *Zootermopsis*. When a colony of two or three secondary reproductives and 40 nymphs of *Z. nevadensis* or *Z. angusticollis* was placed in a clean rectangular Wilson nest (8) at 22°C and a relative humidity of 95 to 100 percent, they invariably built where the lid of the nest was not quite sealed. The first reaction of the termites to this situation was to deposit the fecal cement near the crack. This

same building reaction could be elicited by many different stimuli in experimental colonies of composition similar to that described above, and a dead ant or drops of dilute phenol or of distilled water caused the deposition of fecal cement around or on the foreign substance. In experiments with the ants and the phenol, snapping responses and lunges were made by the termites before fecal material was deposited, and in all experiments building at the site of the foreign material continued until the surface was coated, or in the case of the ants until they were completely buried, the rate of building declining and building finally ceasing. Thus, many substances whose odors differ from that of the termites elicited building, but they also called forth the defensive snapping response.

To see whether building could be induced by a structural rather than a chemical stimulus, I introduced pieces of copper sheeting (1.5 by 7.5 cm) into the nests and left them for a week. At the end of that time fecal pellets and material had been deposited mainly on the edge of the sheeting, thus outlining it. Similar results were obtained with cardboard, though a little fecal material was present in some spots on the main surface. It cannot be supposed that cardboard or gauze is more odorous at its edge. When copper gauze similar in size and shape to the sheeting was used, the results were again comparable, but here the interstices of the gauze were also focuses for the deposition of cement, and the mesh was finally completely filled with fecal material. From these observations and experiments, one can see that many known stimuli can cause building. Sharp edges and crevices, as well as odor, seem to stimulate building. Structure and odor, of course, may in some, or perhaps all, instances be combined.

During this behavior, trail laying and recruitment of other nymphs was noted such as occurs in alarm behavior experimentally induced by active physical disturbance of a termite with a clean flamed needle (6). In my experiments the first nymph to encounter the gauze dragged its abdomen on the ground, an action indicative of trail-laying; it then ran back to the center of the nest and transmitted the alarm by bumping another termite in the characteristic manner. The activity in the present situation could be seen

to be of a much lower degree than that of a termite physically disturbed. The path taken by the alerted termite was traced in ink on the glass cover of the nest; that other termites which were alerted followed this same path to the gauze indicates that a trail had indeed been laid. To get an idea of the rate of recruitment in this experiment, I drew a line in ink on the cover of the nest 1 cm away from and parallel to the gauze. An area (1 by 7.5 cm) was thus delineated adjacent to the gauze. A similar area was formed at the other end of the nest to act as a control. The numbers of nymphs coming into these areas and staying a minimum time of 15 seconds inside, with at least 30 seconds outside before a subsequent re-entry, was noted over a 30-minute period starting when the first nymph encountered the gauze. During this time there were 67 entries into the gauze area while there were nine into the control area. A week later, when the construction was completed, there were only five entries, by a similar count, in the experimental area. Thus, nymphs are recruited to building sites and are recruited by means of a trail being laid.

A hypothesis that can begin to explain the construction behavior of termites can now be put forward. When a nymph of *Zootermopsis* is alarmed experimentally it may either give a snapping response of high or low intensity, or it may deposit fecal cement (6). These responses are graded, in that a high input stimulus (for example, a squashed ant moved on the end of a pair of forceps) elicits snapping, lunging, and a high degree of activity while a low input stimulus (for example, a Wilson nest being unplugged) produces a low level of alarm or excitation usually resulting only in the deposition of some fecal cement. In both cases, just as in my experiment, a nymph lays a trail and recruits other nymphs to the site of alarm. The results of this alarm which are important in relation to my work are this deposition of fecal cement and the beginning of building, in which the recruited nymphs participate. Building behavior is, therefore, considered as one response to a stimulus which alarms the termite. As has been pointed out, many kinds of stimuli will produce alarm and thus will evoke building. The initial stages of building are not uncoordinated as Grassé suggests since the trail is a

directional vector and alarm is transmitted by contact in the usual way (6) so that "builders" are recruited. As mentioned previously, the hypothesis of stigmergy fails to propose a mechanism for the cessation of building. From the aforementioned experiments one can see the elimination of the primary stimulus or cause of alarm provides such a mechanism. When an open exit of a Wilson nest is sealed and the stimulus of steep gradients of odor or humidity, or perhaps of air movement, is removed, building ceases with negative feedback mechanism operating in building behavior. In certain situations various degrees of alarm in the colony follow on each other. For example, an intruding ant will first be killed and immobilized by being bitten by a soldier or nymph, then building will commence, and the remains will be buried. When the burying is completed, the alarm stimulus, in this instance probably odor, is removed completely, and the colony returns to a lower rate of activity (Fig. 1).

It would seem then that building is quite a direct response to danger, its immediate function being a homeostatic one of actively removing the alarming stimulus; the colony then returns to normal until another stimulus situation is encountered. In some instances, the elimination of one stimulus may create a new stimulus situation (for instance, structural); with the aforementioned qualifications and modifications this approximates part of the hypothesis of Grassé.

The completion of the varied types of nests in higher termites could be accounted for in part by such mechanisms, in view of the fact that polyethism has been reported in termites (9) and that the different social interactions within the different species could produce different stimulus situations resulting in different end structures. The postulation of Schmidt (10) and Emerson (1) that a specific nest is the expression of the total behavior of the species and the true interaction between the genome and the environment is thus supported by direct experimental results.

In light of my work Howse's contention that air movement is the definitive stimulus in the nest building and construction behavior of termites could not be supported. While there is no doubt that those insects are extremely sensitive to such stimuli and that they

will be alarmed by small air movements, many stimuli can cause alarm (and thus building) and air movement is only one of such stimuli. On the basis of certain experiments, Howse rejects suggestions (5, 6) that a sharp gradient in humidity might act as a stimulus for the deposition of fecal cement. These experiments, however, assumed that a decrease in humidity is synonymous with a sharp humidity gradient. Howse kept his nymphs of *Zootermopsis* in tubes at relative humidities of 56 and 35 percent as well as at the normal relative humidity (90 to 100 percent) for these animals; he found that building was reduced at the two lower humidities. The results that Howse obtained might be expected, since termites do not thrive in the unnatural conditions of low humidity and their reduced activity in such situations would include reduced building activity. Also, in building, the fluid fecal cement is a necessary component, and one would expect that in an environment with a low humidity the supply of this material would be depleted owing to the animal's conserving water. This depletion would also result in reduced building activity.

Trail-laying and building behavior appear to be responses to alarm and can be thought of as a primitive defense mechanism. This mechanism has evolved in the higher termites and enables them to forage at some distance from the nest. In this regard the suggestion of Grabensberger (11) that the presence of food alarms a termite (*Fütteralarm*) is supported.

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7 April 1967