group B. That only ten patients from a total of 200 (B + C) were in this group strengthens the possibility of coincidence.

Clinically, there is nothing unique about Siegal's patients except that they improved with iodide therapy. This means that they provide us with no common denominator which might allow preselecting of other asthmatic patients who would be appropriate candidates for a controlled study. To undertake a controlled double-blind evaluation of iodides in a large group of unselected asthmatic patients is a formidable task, and probably futile, particularly relative to Siegal's hypothesis. As pointed out by Modell and Houde,[3] there are too many factors at work "immaterial to the specific problem at hand." Shure and St. John[4] brought this out in one of the few controlled studies pertaining to iodide therapy in asthma. They were forced to reduce their series for analysis from 126 to 28 patients to get rid of "background noise"—that is, the reports from patients who were unable to discriminate between one agent and another.

Another approach might be to select patients for a controlled study on the basis of their earlier favorable response to iodide. Even if we disregard the fact that some of Siegal's patients became unresponsive to iodide, their responses, as well as those of other patients who have experienced iodide therapy, would be almost impossible to control. There is an unavoidable bias introduced by the distinctive iodide side effects which cannot be duplicated by placebos. One wonders about this bias also in the improvement reported by some patients in the above-mentioned controlled study.[4]

The problem is compounded when one attempts to evaluate the expectorant action of iodide, which is dose related and closely allied to the other physiologic reactions of iodism.[2] Changes in sputum should at least provide a more objective index of the pharmacodynamic action of iodide. Alas, in controlled studies, the observed effects on sputum viscosity or volume have been unimpressive, and the changes that were observed did not correlate with clinical improvement.[5, 6]

The greatest contribution of this paper is the evidence that iodide therapy is worthless for a majority of asthmatic patients, and may be harmful. Considering the casual, and often routine, use of iodides by some physicians, this deserves repeated emphasis. Asthma is a capricious disease and iodide treatment has capricious effects. Only when the occasional patient shows distinct improvement with potassium iodide, can we justifiably resort to an old empirical rule of therapy, "if the patient is improving, keep using it." However, such a practice has not led to the discovery of any general truths about the nature of asthma or the specific action of iodide. Until dependable methods of evaluation become available, this practice should be subjected to continual critical scrutiny during the long-term management of each patient.

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Dr. George V. LeRoy.—The fact that complete remission of symptoms lasting from 4 months to 5 years occurred in about 5 per cent of 200 asthmatic patients should not surprise anyone. If we exclude from the category of "asthmatics" those patients with documented chronic bronchial disease—and chronic pulmonary disease, we are left with a group who have paroxysmal or persistent asthma the presumptive causes of which include allergy, psychophysiologic reactions, and hypersensitivity of the respiratory system to en-

vironmental agents. We do not expect complete *spontaneous* remission among patients with disease of the bronchi or the lungs. Any amelioration of their asthmatic symptoms ordinarily is associated with rational therapy and is to a certain extent predictable. However, in dealing with the latter category of asthmatic subjects, I am impressed by my inability to predict the course of the condition. At almost any time after its onset, and for reasons that are rarely clear, the symptoms may disappear entirely. The duration of remission is also unpredictable. It is unfortunate that we do not know the probability that spontaneous remission will occur, or the distribution of the durations of remissions. Nevertheless, the fact that remission occurs is a reality, and the presumption that it is spontaneous is supported by a number of considerations. Iodides are not the only drugs which have received credit for a "cure" of asthma. Arsenic, stramonium, bromides, Lobelia, tobacco, vaccines, and many other substances have been mentioned favorably in the literature. Change of occupation, moving to the city—or to the country, strenuous regimens of exercise (walking 20 miles a day), psychotherapy—the list is long—all have "cured" some asthmatic patients. In addition, it is common knowledge that an unspecified fraction of juvenile asthmatics cease to have symptoms after puberty.

Our inability to distinguish between a spontaneous remission and the effect of a drug—such as potassium iodide—makes it virtually impossible to evaluate Siegal's report. Most physicians recognize the pitfalls involved in attempting to attribute the "cure" of a chronic disorder, such as asthma, to a particular regimen. The fact that *post hoc ergo propter hoc* may be fallacious is accepted, and, in an effort to avoid faulty attribution, statistical methods to evaluate evidence have been employed.

It is not easy to design a satisfactory clinical trial to evaluate the effectiveness of individual drugs in bronchial asthma. There are so many variables in the individual case that most workers hesitate to commit themselves to conventional trials of the double-blind variety. Until a new format is devised we are forced to depend upon clinical judgment in respect to drugs, which means that we can only state that a particular regimen appears to be better, worse, or no different than the one it supplants. This, of course, is a *post hoc* judgment which is necessarily provisional.

Siegal carries the *post hoc ergo propter hoc* reasoning one step further than usual and suggests that there may be some fundamental difference between iodide-responsive and iodide-unresponsive asthma. This kind of reasoning is difficult to categorize. Another physician confronted with the same experience might well say: "Since all my asthmatics were treated with enteric-coated tablets of potassium iodide, and since an unexpectedly long remission failed to occur in 95 per cent, some factor *other* than iodide must have been responsible for the complete remissions that occurred in these 10 cases." It is possible that a scrupulous investigation of the lucky 10 might provide insights into factors—other than the conventional drugs—that were responsible for the remission. If, as I suspect, such remissions are spontaneous in the sense that the drugs used are not responsible, it would be most helpful if we knew something more about the process. I have the strong impression that a change, perhaps a subtle one, in the total life-situation of the patient is the single most important factor. Unfortunately, we seldom have sufficient information on which to base such a conclusion before a remission occurs. When the patient is free of symptoms he has no further need of the doctor, and it is virtually impossible to investigate the situation retrospectively.

Future studies of asthma would be benefited if reports such as Siegal's were more complete with respect to diagnosis and details. Some day we may have information on the incidence and distribution of symptom-free periods in patients with bronchial asthma. Until we have such data evaluation of therapy must remain subject to the impressions of the clinician.

Dr. Kenneth P. Mathews.—Especially since there are a limited number of ways in which bronchioles can react, it seems very possible that a variety of circumstances may eventuate in apparent asthma. If so, certain drugs could produce a beneficial effect in some instances but not others. If, as Dr. Siegal suggests, the percentage of cases where conditions are favorable for demonstrating the action of a drug is less than the usual percentage of