Conference on 8-Aminoquinoline Compounds in Relation to Poliomyelitis

Cincinnati, Ohio - March 4, 1949

Purpose: To determine the best possible course to pursue with regard to the preliminary observation that some 8-aminoquinoline compounds may favor the poliomyelitic process while others may interfere with it.

Participants: Dr. Kenneth G. Blanchard, Johns Hopkins University School of Medicine
Dr. Nathan L. Drake, University of Maryland
Dr. Robert G. Elderfield, Columbia University
Dr. Thomas M. Rivers, Hospital of The Rockefeller Institute
Dr. I. G. Schmidt, University of Cincinnati College of Medicine
Dr. L. H. Schmidt, Christ Hospital Institute of Medical Research
Dr. H. M. Weaver, National Foundation for Infantile Paralysis

Place of Conference: Laboratory of Dr. A. B. Sabin, at The Children's Hospital Research Foundation

Summary of Discussion and Decisions:

Dr. L. H. Schmidt presented a summary of the work (published and unpublished) done by himself and Dr. I. G. Schmidt on the relationship between chemical composition and configuration of 8-aminoquinoline compounds and their neuronotoxic properties. The 3 major types of toxic reactions following the administration of 8-aminoquinoline compounds to rhesus monkeys are: 1) effects on the central nervous system, 2) effects on heart and circulation, and 3) effects on formed elements of peripheral blood and bone marrow. He pointed out that the composition of the aliphatic side-chain, both as regards the radicals attached to the terminal amino group and the number of carbons between the two
amino nitrogens, was most important in determining the effects of a given 8-
aminoquinoline compound on the nervous system. However, he listed a number of
exceptions in which various substituents on the quinoline ring were capable
either of depriving a markedly neuronotoxic compound of its effect on the ner-
vous system or of greatly modifying it. The addition of a methyl group in the
4-position or of a methoxy group in the 2-position on the quinoline ring were
some of the ways in which neuronotoxicity could be modified without altering
the composition of the aliphatic side-chain.

Dr. Sabin reported on the effects of 4 compounds (plasmocid,
methyl plasmocid, pentaquine and isoplasmocid) on poliomyelitis in monkeys and
mice, and a separate summary of his remarks is appended. Drs. Elderfield, Drake
and Schmidt following a conference they had the preceding day on the method
of preparation of the compound called "isoplasmocid" reached the conclusion
that the precise chemical configuration of the material which gave the promising,
antagonistic effects on poliomyelitis in monkeys was in doubt. It was decided,
therefore, that the first job that had to be done was to determine whether the
"isoplasmocid" that was used was indeed a 2-methoxy isomer of plasmocid or
another compound of the type indicated in the table attached to Dr. Sabin's
summary, or a mixture. (Homogeneity tests completed that day in Dr. Schmidt's
laboratory indicated that the compound used was not a mixture of 2 substances.)
Dr. Elderfield undertook the job of working out the structural formula of the
"isoplasmocid," and he expressed the belief that he would be able to complete
the job in a matter of weeks. It was generally agreed that having determined
the structural formula of the "antagonistic" compound, it would be desirable
to synthesize more of it as well as three or four analogues in which the sub-
stituent in the 2-position on the quinoline ring and the aliphatic side-chain
were varied. After preliminary pharmacological study to determine the approximate ID<sub>50</sub> and maximum tolerated dosage, it was thought that these compounds should be tested for their effect on poliomyelitis in monkeys. The results of these tests, it was believed, would provide information to indicate whether or not a given chemical composition or configuration of certain 8-aminoquinoline compounds could consistently interfere with the poliomyelitic process in the monkey to a degree, that would justify further systematic work with this group of compounds. Drs. Elderfield and Drake undertook the task of synthesizing the desired compounds, Dr. Schmidt, the task of pharmacological processing, and Dr. Sabin, the task of determining their value in poliomyelitis. It was decided that the proposed job would be regarded as a cooperative investigation, the results of which would be published with all the participants as co-authors.