Over the past four and a half years, Circulation Research has undergone a remarkable transformation. Among the >40 changes that we have made to the journal is the introduction of a cornucopia of new article categories (17 of them thus far; Table). We believe that this massive infusion of new content has enriched Circulation Research, making it more interesting and invaluable to the cardiovascular research community. In our incessant quest for ideas that will further improve the journal and provide a forum for new types of scientific communication, we are now introducing yet another article category: New Hypotheses in Clinical Medicine.

The process of discovery in clinical research is quite different from that in basic research. While in the latter it is possible (and, indeed, customary) to formulate a hypothesis, design an appropriate experiment, and collect data that enable the investigators to either accept or reject the working hypothesis with a reasonable degree of certainty, such a conclusive test is much more difficult (and expensive), and often not even feasible, when it comes to clinical studies. Inherent in all human studies is the difficulty in achieving direct evidence for or against a given hypothesis, particularly when the hypothesis involves the mechanism or pathophysiology of a disease (as opposed to, say, its treatment or prognosis). It is not a coincidence that the most common complaint voiced by reviewers of clinical manuscripts is that the work is descriptive and typically fails to illuminate the mechanism of the disease or therapy being studied.

Experience teaches us that conclusive proof of hypotheses pertaining to clinical medicine, especially when they involve a mechanism of disease, requires many successive steps (i.e., independent studies in different populations and with different techniques). Seldom does one clinical study conclusively prove or disprove a hypothesis; and when that study is the first to propose a hypothesis, it almost never provides conclusive evidence. In clinical research, the process of validating a concept is typically long and slow. Nevertheless, it is crucial that this process be started. The beginning of the process is a hypothesis, which is usually formulated on the basis of small, preliminary studies, and inconclusive observations.

New hypotheses are the engine that drives medical progress. Although the studies that support a new hypothesis are frequently preliminary or retrospective, their dissemination in the scientific literature is, nevertheless, necessary to put in motion the process of validation, in which the idea is then tested in more rigorous, comprehensive, and conclusive investigations.

With these considerations in mind, we are launching this article category to provide a forum for clinical papers that propose a new hypothesis on the etiology, pathogenesis, or treatment of human disease. Novelty is paramount. The evidence supporting the new hypothesis may not be robust, but it must be sufficiently cogent to render the hypothesis plausible and worthy of further investigation. Hypotheses predicated on conjectures, speculations, personal opinions, anecdotal experience (case reports), or “unpublished observations” will not be considered for this category. The typical study that would fit New Hypotheses in Clinical Medicine is an initial, pilot (preliminary) investigation in a small patient population, in which careful observations suggest, but do not prove, a new mechanism or pathogenesis. Another example would be a retrospective analysis of a data set that reveals a previously unrecognized pattern, warranting prospective analyses. In either case, the observations should be intriguing enough to warrant more systematic studies.

New Hypotheses in Clinical Medicine is the 18th new article category to appear in Circulation Research since 2009 (Table). This category is inaugurated in the current issue of
the journal with the article by Nadkarni et al., who propose that neutrophils may play a pathogenic role in giant-cell arteritis. Although the study was conducted in a small group of patients and many questions remain unanswered, the evidence presented is consistent with this new, intriguing idea, which will need to be verified in future investigations.

The introduction of New Hypotheses in Clinical Medicine is another manifestation of the editors’ interest in making Circulation Research a forum for clinical studies that help us understand the etiology, pathogenesis, pathophysiology, and treatment of human disease. Although we expect most of these articles to be preliminary, we hope that they will stimulate further studies to confirm or reject the hypotheses put forth.

Disclosures
None.

References

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