Harper's Magazine made its debut in June 1850, the brainchild of the prominent New York book-publishing firm Harper & Brothers. The initial press run of 7,500 copies sold out immediately, and within six months circulation had reached 50,000.

Although the earliest issues consisted largely of material that had already been published in England, the magazine soon began to print the work of American artists and writers — among them Winslow Homer, Frederic Remington, Edward Penfield, Henry James, Mark Twain, and Jack London. Several departments served to note regularly important events of the day, such as the publication of Herman Melville's new novel, Moby-Dick; the laying of the first trans-Atlantic cable; the latest discoveries from Thomas Edison's workshop; or the progress of the crusade for women's rights.

In more recent years, the magazine published Woodrow Wilson and Winston Churchill long before either man became a political leader. Theodore Roosevelt wrote for Harper's, as did Henry Stimson when he defended the bombing of Hiroshima. In the 1970s, Harper's Magazine broke Seymour Hersh's account of the My Lai massacre and devoted a full issue to Norman Mailer's “The Prisoner of Sex.”

Over the years, the magazine's format has been revamped, its general appearance has evolved considerably, and ownership has changed hands. In 1962, Harper & Brothers merged with Row, Peterson & Company to become Harper & Row (now HarperCollins.) Some years later the magazine became a separate corporation and a division of the Minneapolis Star and Tribune Company. In 1980, when the parent company announced that Harper's Magazine would cease publication, John R. (Rick) MacArthur and his father, Roderick, urged the boards of the John D. and Catherine T. MacArthur Foundation and the Atlantic Richfield Company to make a grant of assets and funds to form the Harper's Magazine Foundation, which now operates the magazine.

In 1984, Harper's was completely redesigned by long-time editor Lewis H. Lapham and MacArthur, who had become publisher of Harper's Magazine and president of the Foundation. Recognizing the time constraints of the modern reader, the revived magazine introduced such original journalistic forms as Harper's Index, Readings, and Annotation to complement its acclaimed fiction, essays, and reporting. The quarterly Folio section, introduced in 1992, showcases exemplary works of journalism and fiction at lengths of 16 pages or more. In 1994 the magazine was honored with a record three National Magazine Awards, for excellence in feature writing, essays & criticism, and fiction. It has since gone on to win 9 more.

June, 2010, welcomed a new chapter in the glorious history of America's oldest, continuously published monthly magazine. Mr. Lapham was appointed editor emeritus and long-time staff member Ellen Rosenbush was named as Harper's next editor, the first woman to hold the position.