Current Comments

Most-Cited Articles of the 1960s. 4. Clinical Research

Number 6

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With this essay, we conclude our study of the most-cited science articles of the 1960s. Previous essays have discussed highly cited articles in the physical sciences, 1 biochemistry and molecular biology, 2 and preclinical areas 3 for that decade. Now we take a look at clinical research.

As I pointed out before, these lists were compiled from the Science Citation Index® (SCI®) data base for the years 1961 to 1978. It bears repeating that limiting the study to the 100 mostcited articles was arbitrary. The list could have been extended further if time and energy allowed. Furthermore, there has been no effort to identify purely clinical work. Rather, these are the papers, out of a group of 400 in this series, that are most readily classified as "clinical." Indeed, the relatively small percentage of papers from purely clinical journals emphasizes this artifact. Therefore, I do not mean to imply that the 100 articles shown in Figure 1 necessarily are the "best" clinical research articles of the 1960s. Nevertheless, I'm sure that many of these articles have made significant contributions to the development of their respective fields.

How do you separate articles in "clinical" medicine from other articles in medical research, especially when many of the papers appear in the same journals? You ask for help from experts, although eventually you make some arbitrary decisions. Even the decision to list all papers cited by the given threshold is arbitrary. In any case they were all heavily cited.

To discourage comparisons of citations to individual papers, we alphabetized the listings under each subject area. This is the same procedure we followed in the other essays in this series.

Each of the papers on this list was cited at least 345 times. Compare this to our list of the 100 most-cited preclinical papers. There, the least cited paper received 521 citations.³ Similarly, each article on our list of physical science papers received at least 500 citations.¹ Thus, it would appear that super-cited papers in clinical research receive fewer citations than do papers in the other categories in this series. On average, preclinical papers cite and are cited by more papers than are clinical papers. In biochemistry the average number of references per paper now exceeds 27.⁴

The average clinical article on our list received 644 citations. This means it was cited about 36 times per year during the 18-year period. By way of comparison, the average paper published in a journal covered by the SCI received 3.28 citations during that period.

The articles presented here were published in the 47 journals listed in Table 1. More than a quarter of the papers were published in just four journals: Journal of Clinical Investigation, Journal of Experimental Medicine, Lancet, and New England Journal of Medicine. All but two of the papers were written in English. The papers by M. Eggstein and H. Ehringer were written in German. The absence of journals like the British Medical Journal (BMJ) emphasizes the bias in this list. It is well-

Table 1: Journals that published the most-cited 1960s articles listed in Figure 1.

1960s articles listed in Figure 1.	
J. Clin. Invest.	10
J. Exp. Med.	6
Lancet	6
New Eng. J. Med.	6
J. Clin. Endocrin. Metab.	5
Proc. Nat. Acad. Sci. US	5
Science	5
J. Am. Med. Ass.	
J. Lab. Clin. Med.	3
Am. J. Clin. Pathol.	2
Am. J. Med.	2
Blood	2
Circulation	2
Clin. Chem. Acta	2
J. Appl. Physiol.	2
J. Clin. Pathol.	4 3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Klin. Wochenschr.	2
Nature	2
Pediatrics	2
Physiol. Rev.	2
Scand. J. Clin. Lab. Inv.	
Acta Med. Scand.	1
Acta Physiol. Scand.	1
Adv. Immunol.	1
Am. Heart J.	1
Am. J. Psychiat.	1
Anal. Biochem.	1
Ann. Intern. Med.	1
Biochem. J.	1
Can. Med. Ass. J.	1
Circ. Res.	1
Endocrinology	1
Exp. Cell Res.	1
J. Allergy Clin. Immun.	1
J. Atheroscler. Res.	1
J. Bacteriol.	1
J. Immunol.	1
J. Neurol. Neurosurg. Psychiat.	1
J. PhysiolLondon	i.
Metabolism	1
Mod. Conc. Cardiov. Dis.	1
Pharmacol. Rev.	1
Psychol. Monogr.	1
Psychol. Rep.	1
Prog. Allergy	1
Transplantation	1
Transplant. Rev.	1

known, for example, that Lancet attracts many important papers in medical genetics. In a future study, I will list the most-cited articles in BMJ and other clinically oriented journals.

Almost a quarter of the papers (23) were single-author works. Twenty-nine had two authors, 20 had three, 20 had four, four had five, and two had six authors. There were two with eight authors. Sixteen of the papers have appeared as Citation Classics in Current Contents. 5

Twenty-four authors contributed two or more papers to the list. S.A. Berson, S.O. Freedman, P. Gold, and R.S. Yalow authored three papers. Two articles each were authored by P. Astrup, B.S. Blumberg, G.V.R. Born, G.C. Cotzias, K. Engel, S.M. Glick, G. Henle, and W. Henle. Also contributing two articles were C.W. Gottlieb, E. Haber, V. Herbert, O. Hornykiewicz, K. Jørgensen, K.S. Lau, A.R. Midgley, B.E.P. Murphy, J. Roth, O. Siggaard-Anderson, P.I. Terasaki, and T.B. Tomasi. A total of 239 authors appear on the list.

Seventy-six institutions are represented in this study. They are shown in Table 2, along with the number of authors who appear on our list of 100 papers. The number of papers from each institution is also indicated. Just seven institutions account for about 40 percent of the authors listed. Fifty-two of the 76 institutions are in the US. Nine institutions are in the UK, four are in Sweden, and three are in Canada. France, New Zealand, and the Federal Republic of Germany each have two institutions on the list. Denmark and Austria have one each.

McGill University and affiliated institutions in Montreal account for as many papers as the NIH! Two authors who contributed three papers to the list, P. Gold and S.O. Freedman, are affiliated with McGill University.

Three of the authors were Nobel prize winners. B.S. Blumberg won the prize in 1976 for his work on hepatitis. R.S. Yalow won the prize in 1977 for her work on radioimmunoassay. Both of these authors published highly cited papers before winning their awards. P.B. Medawar was presented the prize in 1960 for his work in acquired immunity. He continues to be highly cited both for his 1966 paper with R.H. Levey as well as for his earlier work.

The list is divided into 13 categories: immunology; endocrinology; cardiopulmonary medicine; clinical chemistry and pathology; hematology; cancer; psychiatry, psychology, and psychopharmacology; allergy; clinical genetics;

Table 2: Institutional affiliations of authors of the most-cited 1960s articles according to number of papers. The number of authors from each institution is indicated in parentheses.

National Institutes of Health		8	(24)	
National Heart Institute	(9)			
Lab. Virol. & Immunol.	(6)			
National Institute of Arthritis & Metabolic & Digestive Diseases National Institute of Child Health & Human Development	(3) (3)			
Department unspecified	(2)			
National Institute of Mental Health	(1)			
McGill University, Montreal, Canada	(-)	8	(22)	
Royal Victoria Hospital	(11)		(/	
McGill University Clinic, Montreal General Hospital	(7)			
Department Invest. Med.	(2)			
Department Physiol.	(2)			
University of California		6	(13)	
School Med. Los Angeles	(8)			
San Francisco Med. Ctr.	(3)			
School Med. San Diego Harvard Medical School	(2)	6	(10)	
Rockefeller University, New York, NY		4	(10) (8)	
Univ. Pennsylvania Sch. Med., Philadelphia, PA		4	(4)	
Columbia Univ. Coll. Phys. & Surg., New York, NY		3	(5)	
Inst. Cancer Research, Philadelphia, PA		3	(8)	
Johns Hopkins Sch. Med., Baltimore, MD		3	(6)	
Massachusetts General Hosp.		3	(3)	•
Mt. Sinai Hospital, New York, NY		3	(8)	
Rigshospitalet, Copenhagen		3	(10)	
University of Washington, Seattle, WA		3	(10)	
Veteran's Hospital Radioisotope Service, New York, NY		3	(10)	
Brookhaven Nat. Lab., Upton, NY Childen's Hore of Philadelphia		2	(6) (3)	
Children's Hosp. of Philadelphia Creighton Univ. Sch. Med., Omaha, NE		2	(2)	
New York Univ. Sch. of Medicine		2	(3)	
Postgraduate Med. Sch. of London		2	(5)	
Queen Mary Vet. Hosp., Montreal, Canada		2	(2)	•
Royal College of Surgeons of England, London		2	(3)	
SUNY		2	(5)	
New York	(3)			
Buffalo	(2)	_		
University of Colorado Med. Ctr.		2	(5)	
University of Lund, Sweden		2	(3) (2)	
Univ. of Michigan, Ann Arbor, MI University of Minnesota Med. Sch.		2	(5)	
University of Vienna, Austria		2	(3)	
Bland-Sutton Inst. of Pathol., Middlesex Hosp., London		1	(3)	
Boston City Hospital		1	(1)	
Boston University Med. Sch.		1	(2)	
Peter Bent Brigham Hosp., Boston, MA		1	(4)	
Case Western Reserve Sch. Med., Cleveland, OH		1	(1)	
Children's Hosp. Med. Ctr., Boston, MA		1	(1)	
Christchurch Hosp., Christchurch, New Zealand		1	(1)	
City of Hope Med. Ctr., Duarte, CA		1	(3)	
Cleveland Clinic, Cleveland, OH F. Delafield Hosp., New York, NY		1	(2) (1)	
Albert Einstein College Med., New York, NY		i	(2)	
Fitzsimmons Army Hosp., Denver, CO		i	(1)	
Hosp. Paul-Brousse, Villejuif, France		1	(4)	
Hôtel-Dieu Hosp., Montreal, Canada		1	(4)	
Inst. Gustav Roussy, Villejuif, France		1	(4)	
Jewish Hosp., New York, NY		1	(1)	
Kansas State Univ., Manhattan, KS		1	(1)	
King Gustaf V Research Inst. & Dept. Int. Med., Karolinska Inst., Stockholm, Sweden		1	(1)	
Med. Univ. Marburg, Fed. Rep. Germany		1	(1)	
Med. Univ. Tubingen, Fed. Rep. Germany		1	(1)	
National Institute Med. Res., London New York Blood Ctr., New York, NY		1	(2) (1)	
New York Hosp./Cornell Med. Ctr., New York, NY		1	(1)	
Newton-Wellesley Hosp., Newton, MA		i	(3)	
Ohio State Univ. Coll. Med., Columbus, OH		i	(3)	
Presbyterian Hosp., New York, NY		1	(1)	
Queen Victoria Hosp., Sussex, UK		1	(1)	
Royston Hospital Lab., Hastings, New Zealand		1	(2)	
St. Mary's Hosp., London		1	(1)	
Tufts Univ. Sch. Med., Boston, MA		1	(1)	

Univ. of Cambridge, Cambridge, UK	1	(2)
Univ. of Conn., Storrs, CT	í	(1)
Univ. of Göteborg, Sweden	i	(i)
Univ. of Leeds, UK	1	(1)
Univ. of Miami Sch. Med.	1	(1)
Univ. of Minn. Hosp., Minneapolis, MN	1	(1)
Univ. of North Carolina Sch. of Med., Chapel Hill, NC	1	(1)
Univ. of Southern California Med. Sch., Los Angeles, CA	1	(2)
Univ. of Vermont Coll. Med., Burlington, VT	1	(2)
Univ. of Wisconsin, Madison, WI	1	(2)
Uppsala University, Sweden	1	(3)
US Public Health Service Hospital, New York, NY	1	(6)
VA Central Neuropsychiat. Res. Lab., Perry Point, MD	1	(1)
VA Hospital, Seattle, WA	1	(2)
VA Hospital, Houston, TX	1	(1)
Wellcome Res. Labs., Kent, UK	1	(1)
Willowbrook State School, New York, NY	1	(1)
Wistar Inst. Anat. & Biol., Phila., PA	1	(1)
Wood VA Hosp., Milwaukee, WI	1	(2)

*Second affiliation for a single authored paper.

neurology; gastroenterology; and pediatrics. Three papers on the list do not fit neatly into any of the previous subject categories so they are described as miscellaneous.

Twenty-one papers on the list are from the field of immunology. Most-cited among them is the paper by K.K. Mittal and colleagues. That paper deals with organ transplantation, as do several other papers in this group.

Sixteen papers were from clinical endocrinology, including two papers on protein-binding by B.E.P. Murphy. The paper by C.N. Hales and P.J. Randle, which describes an immunoassay of insulin, received more than 2,000 citations. Only about 50 papers in the history of science have been cited more than 2,000 times.

Eleven papers fall within the category of clinical chemistry and pathology, including the most-cited paper on the list. D.S. Fredrickson, R.I. Levy, and R.S. Lees' "Fat Transport in Lipoproteins-An Integrated Approach to Mechanisms and Disorders" received 5,138 citations during the 18-year period. However, this article was published in five parts: part one receiving 1,241 citations, part two 937, part three 1,037, part four 953, and part five 970. The number of papers citing the article is far less than the number of citations because one paper could have cited all five parts. From a comparison of the citations to the different parts, we estimate that approximately 1,800 different papers cited the article.

Fredrickson, Levy, and Lees' paper discussed two methods of separating lipoproteins, combinations of lipids and proteins. Levy has written, "One...of the reasons for the volume of citation received by our articles is that they drew attention to an important group of diseases [hyperlipoproteinemia] that are common and often potentially fatal."6

The field of cardiopulmonary medicine contributed 11 papers to the list, indicating the long-term clinical interest in heart diseases.

Nine papers on the list fall under the heading of hematology. Of note in this group are two papers by G.V.R. Born dealing with the aggregation of blood platelets. Born's 1962 paper introduced "aggregometry," a method for quantifying platelet reactions.

Eight papers were classified under the heading of cancer. The three papers on which P. Gold and S.O. Freedman appear as authors discuss cancer of the digestive system. Three other papers in this group discuss cancer of the lymphatic system.

Psychiatry, psychology, and psychopharmacology contributed six papers to the list. Four of them also appeared on our list of the 100 most-cited articles selected from our Social Sciences Citation Index TM (SSCITM). 7 This is not sur-

^{**}One of the authors represents a second affiliation for a single authored paper.

prising since both the SCI and the SSCI cover psychiatry and experimental psychology.

Five clinical genetics papers appear on the list. The most-cited among them is P.S. Moorhead's paper, which describes a method for preparing the chromosomes of white blood cells for study.

Three allergy papers appear here. The article by L.M. Lichtenstein and A.G. Osler discusses the release of histamine from white blood cells upon exposure to pollen antigen. A. Szentivanyi's paper is on bronchial asthma. The paper by L. Wide and colleagues discusses allergy diagnosis.

There are three papers under neurology, including two by G.C. Cotzias on the treatment of Parkinson's disease. The fields of gastroenterology and pediatrics each contributed two papers to the list.

We hope that these studies of the scientific literature of the 1960s will provide students and others with a useful reminder of some of the work of that decade that has had particularly longlasting impact. Biomedical research is a large-scale activity. To provide a complete picture of just the high-impact work, one would have to list several thousand articles. For this reason, I look forward to the publication of our

Atlas of Science.⁸ In it, we hope to identify almost every significant paper in every field. The first installment of this Atlas is scheduled for completion during the coming year. Not only will key papers and clusters be identified, but they will be briefly "reviewed" by qualified scientists.

There has been some speculation that the change in research funding in the US may have shifted the balance of American impact on international science. Of the 400 papers in our studies of the 1960s, 73 percent were authored by Americans. It will be interesting to observe whether there is a significant change in the percentage of superstar papers published by American scientists in the 1970s. Alternatively, one would hope that larger commitments to basic research in other countries may have increased their contribution of superstar papers enough to affect their percentage. Science is international, and breakthroughs are welcome wherever they occur. These questions will be the subject of future investigations at ISI®.

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Figure 1: 100 most-cited articles of the 1960s in clinical medicine. Authors' affiliations follow each citation. If an article has appeared as a Citation Classic, a reference follows the author affiliation.

Total Citations 1961-1978

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