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TRACKING TRENDS & PERFORMANCE IN BASIC RESEARCH

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WHAT'S HOT IN... MEDICINE, May/June 2010
Pandemic Influenza 2009: The Early Observations

by David W. Sharp



Prominent among this publication's recent listing of the "red-hot research papers" of 2009 are reports, in the astrophysics literature, from something called the Wilkinson Microwave Anisotropy Probe (*Science Watch*, March/April 2010). However, not far behind lie three publications that might be considered of rather more immediate earthly interest. They are on "swine flu, not perhaps the best term for the disease that has swept the world since pandemic H1N1/09 influenza virus first attracted attention just over a year ago.

For one thing, influenza in pigs has long been a worry for animal husbandry without (usually) transmission to humans. For another, H1N1/09 has not (yet) caused outbreaks in swine—but if it did an alarming "Pandora's box" might be opened (J. Cohen, *Science*, 325[5937]: 140-1, 2009).

Paper #2 in the current Medicine Top Ten, from the Novel Swine-Origin Influenza A (H1N1) Investigation Team, wound up 7th among 2009's most-cited publications. At #14 (having finished 18th in the 2009 tally) is a study from the WHO Rapid Pandemic Assessment Collaboration (C. Fraser, *et al.*, *Science*, 324[5934]:1557-61, 2009; total cites 81, latest count 40). Another large collaboration is currently at #15 among medicine's hottest (#39 on the other list): R.J. Garten, *et al.*, *Science*, 325[5937]: 197-201, 2009; total cites 60, latest count 40.

Those three reports are the early fruits of an international cooperative effort triggered by the identification, in mid-April 2009, of two patients in California infected with a novel influenza A virus. Within two weeks of the identification of this virus both the World Health Organization (WHO) and the U.S. authorities had declared a public-health emergency. By the end of that April WHO had already raised the global pandemic alert to phase 5 (out of six). The genomic make-up of the virus meant that the then current vaccine was unlikely to offer protection.

Dr. Fatimah S. Dawood and colleagues (paper #2) record details of the first 642 U.S. cases. The dominant symptoms were fever, cough, and sore throat but a quarter of patients had diarrhea and vomiting. Three-fifths of patients were under 19 years of age. The paper notes that numbers of laboratory-confirmed cases probably underestimate total infections. Although 22 patients in this series required hospital care (and two of them died), influenza is usually self-limited and self-treated and medical help is not sought.

This point is confirmed in a large seroepidemiological study from England (E. Miller, *et al.*, *Lancet*, 375[9720]: 1100-8, 2010), suggesting that infections outnumber estimates from clinical surveillance by a factor as high as 10. The English experience also confirms the vulnerability of children. Interestingly, serum samples from before April 2009 showed that 23% of adults over 65 had protection against the new virus.

Of the other two papers, in *Science*, the one by Prof. Christophe Fraser and colleagues (#14) focuses on the virus's pandemic potential (see also *PLoS Curr Influenza* RRN 1135, 2009[Dec 16]). A key figure is the number of cases one case generates (here



Colorized negative stained transmission electron micrograph (TEM) depicted some of the ultrastructural morphology of the A/CA/4/09 swine flu virus.

From *ScienceWatch.com*, view the [Special Topic of H1N1](#).

1.2 to 1.6, depending on the method used). The data come from Mexico, where the disease seems to have started, and indicate that between 14 and 73 generations of human-to-human transmission had occurred in that country by late April 2009.

Transmissibility for this infection is much higher than that for seasonal influenza, a fact that contributed to WHO's upgrading of the pandemic status. It is more the antigenic and genetic features of swine-origin 2009 A (H1N1) that are the focus in #15. Again, the findings fuel anxiety for the future. Circulation in humans of an influenza virus with an "antigenically and genetically divergent HA [hemagglutinin] and a previously unrecognized genetic composition is of concern to public health officials around the world."

In the U.K. pandemic influenza A (H1N1) has dropped right out of the news, despite a predictable second peak last October.

The National Pandemic Flu Service closed in February 2010, and both here and in the U.S. the most recent official figures show small infection numbers. The epidemiological and virological data in #2, #14, and #15, however, argue against any complacency. ■

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Medicine Top 10 Papers

Rank	Paper	Citations This Period (Nov-Dec 09)	Rank Last Period (Sep-Oct 09)
1	J. Yu, <i>et al.</i> , " Induced pluripotent stem cell lines derived from human somatic cells ," <i>Science</i> , 318(5858): 1917-20, 21 December 2007. [Genome Ctr. Wisconsin, Madison; U. Wisconsin, Madison] *243HE	93	1
2	Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team (F.S. Dawood, <i>et al.</i>), " Emergence of a novel swine-origin influenza A (H1N1) virus in humans ," <i>New Engl. J. Med.</i> , 360(25): 2605-15, 18 June 2009. [Writing group: Ctrs. for Disease Control & Prevent., Atlanta, GA] *458WR	81	†
3	The ADVANCE Collaborative Group (A. Patel, <i>et al.</i>), " Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes ," <i>New Engl. J. Med.</i> , 358(24): 2560-72, 12 June 2008. [Writing Group: 18 institutions worldwide] *311IJ	76	3
4	The ACCORD Study Group (H.C. Gerstein, <i>et al.</i>), " Effects of intensive glucose lowering in type 2 diabetes ," <i>New Engl. J. Med.</i> , 358(24): 2545-59, 12 June 2008. [Writing Group: 10 U.S. and Canadian institutions] *311IJ	73	2
5	R.R. Holman, <i>et al.</i> , " 10-year follow-up of intensive glucose control in type 2 diabetes ," <i>New Engl. J. Med.</i> , 359(15): 1577-89, 9 October 2008. [6 U.K. institutions] *358FS	52	5
6	I.H. Park, <i>et al.</i> , " Reprogramming of human somatic cells to pluripotency with defined factors ," <i>Nature</i> , 451(7175): 141-6, 10 January 2008. [Harvard Med. Sch., Boston, MA; Harvard Stem Cell Inst., Boston, MA] *249GA	50	10
7	J.M. Llovet, <i>et al.</i> , " Sorafenib in advanced hepatocellular carcinoma ," <i>New Engl. J. Med.</i> , 359(4): 378-90, 24 July 2008. [22 institutions worldwide] *329FK	48	7
8	The ONTARGET Investigators (S. Yusuf, <i>et al.</i>), " Telmisartan, ramipril, or both in patients at high risk for vascular events ," <i>New Engl. J. Med.</i> , 358(15): 1547-59, 10 April 2008. [Writing committee: 5 institutions worldwide] *285NK	47	†
9	W. Duckworth, <i>et al.</i> , " Glucose control and vascular complications in veterans with type 2 diabetes ," <i>New Engl. J. Med.</i> , 360(2): 129-39, 8 January 2009. [11 U.S. institutions] *391UG	47	†
10	K. Miller, <i>et al.</i> , " Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer ," <i>New Engl. J. Med.</i> , 357(26): 2666-76, 27 December 2007. [9 U.S. and Canadian institutions] *245UO	45	6

SOURCE: Thomson Reuters Hot Papers Database. Read the Legend.

KEYWORDS: Influenza, swine flu, H1N1, flu outbreak, swine-origin influenza, WHO, flu pandemic.

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