

Point-of-care (rapid) tests for the diagnosis of influenza infection

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Point of care tests

- Tests that are simple and robust, and can be reliably performed at the bedside by staff with minimal training
- Also called rapid tests, near patient tests
- Intended to address some of the issues related to laboratory-based testing especially accessibility and turnaround times.

Why use POC tests?

- Assist in early management of individual cases
 - Guide investigation, treatment, prophylaxis, infections control
- Identify public health problems
- Provide testing in settings without conventional laboratory facilities
- Cheaper than conventional tests in some cases

Those in current use

- IgM detection for dengue
- HIV antibody testing
- Antigen detection tests for influenza
- Antigen detection tests for RSV

Antibody tests

Evaluation of Two Rapid Immunochromatographic Assays for Diagnosis of Dengue among Vietnamese Febrile Patients

Nga TTT et al. Clin Vaccine Immunol. 2007;14:799–801.



		Pan Bio Duo Cassette		SD Bioline Strip	
		Sensitivity	Specificity	Sensitivity	Specificity
Acute	IgG	70.0%	88.3%	ND	ND
	IgM	54.3%	69.7%	ND	ND
Convalescent	IgG	66.4%	94.4%	90.4%	88.9%
	IgM	67.3%	91.7%	10.6%	99.0%

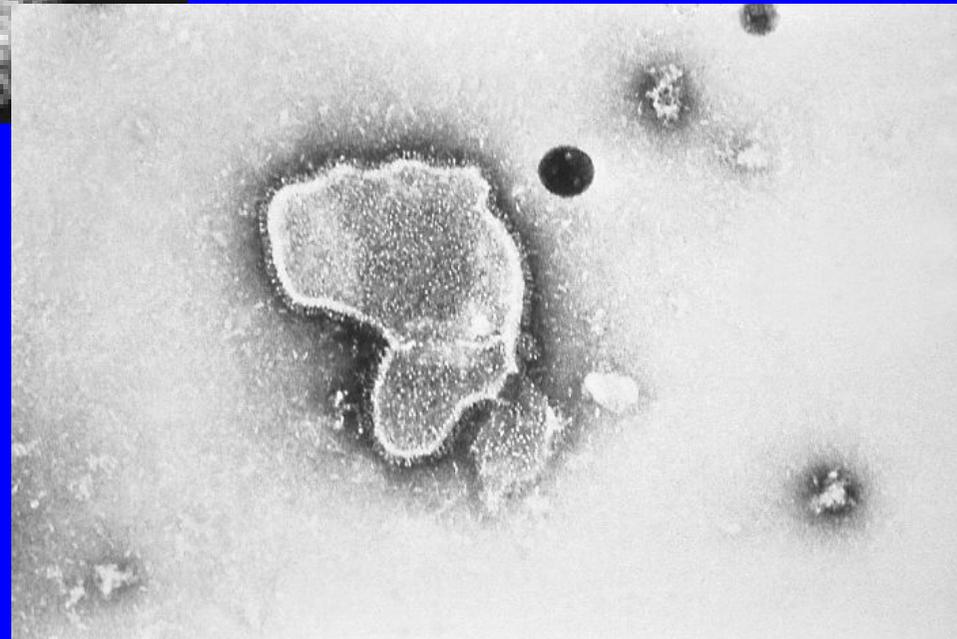
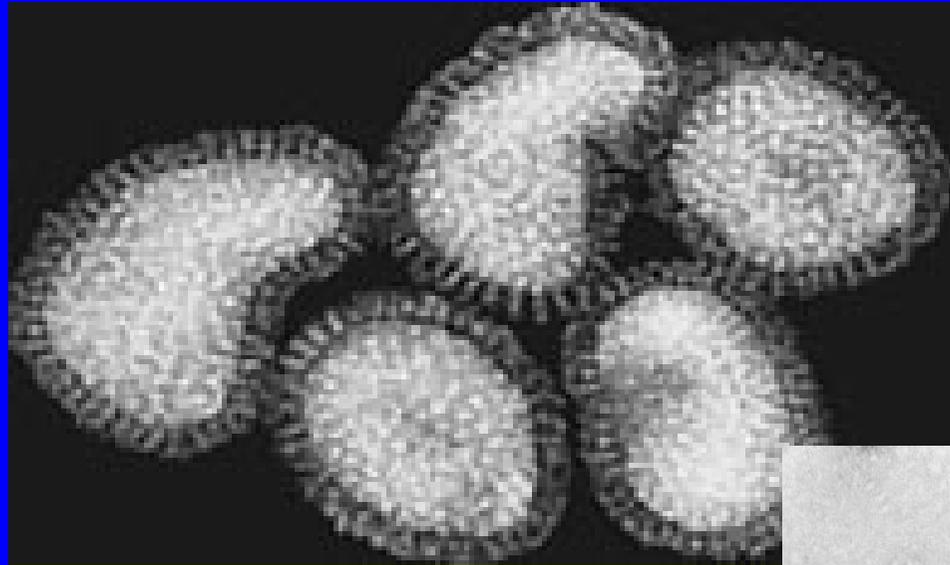
“In conclusion, the PanBio cassette and SD strip tests for dengue infection are easy to use with clear results. They show a high specificity with poor sensitivity, especially with respect to the detection of IgM.”

POC for HIV

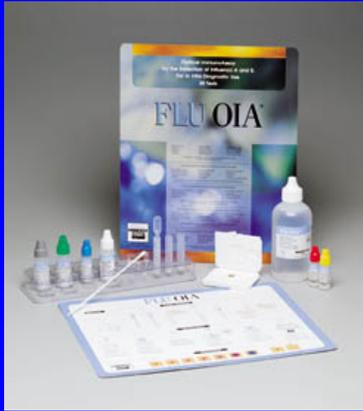
- WHO advocating use in developing countries without access to conventional tests
 - Use of EIA combinations to avoid Western blots and/or NAD testing. Produces results similar to EIA plus WB.
- Community screening programs in “at risk” populations who do not access conventional medical systems
 - Improves testing rates, allows “on the spot” counselling, contact tracing and referral
 - Potential problems with self-testing: dealing with positive results, concealing positive results, etc



Antigen tests



Point-of-care tests for influenza



- Large number on the market
 - some separate influenza A from influenza B
 - some specific for influenza H5
- Detect either antigen or neuraminidase activity
- Vary in the number of steps (4-8) and in the time to perform the test (10-30 mins)

POC tests for influenza detection

		Age	Specimens	Sens vs cult	Sens vs PCR	Specificity
Chan et al	Directigen A/B	80% ≤ 6yo	NPA		A 96% B 87.5%	A 99.6% B 96.8%
Ruest et al	Directigen A/B	Adults & children	NPA	Adults 83% Children ≤ 5yo 95%	Adults 71% Children ≤ 5yo 95%	97-98%
Ruest et al	Quick Vue	Adults & children	NPA	Adults 86% Children ≤ 5yo 95%	Adults 76% Children ≤ 5yo 96%	90%
Noyola et al	Z Stat Flu	Children	Nasal wash	A 76.4% B 40.9%		92.4%
Reina et al	Directigen A/B	Adults & children	Throat swab for adults NPA for children	Adults A 72.7% B 41.1% Children A 86.6% B 62.5%		100%

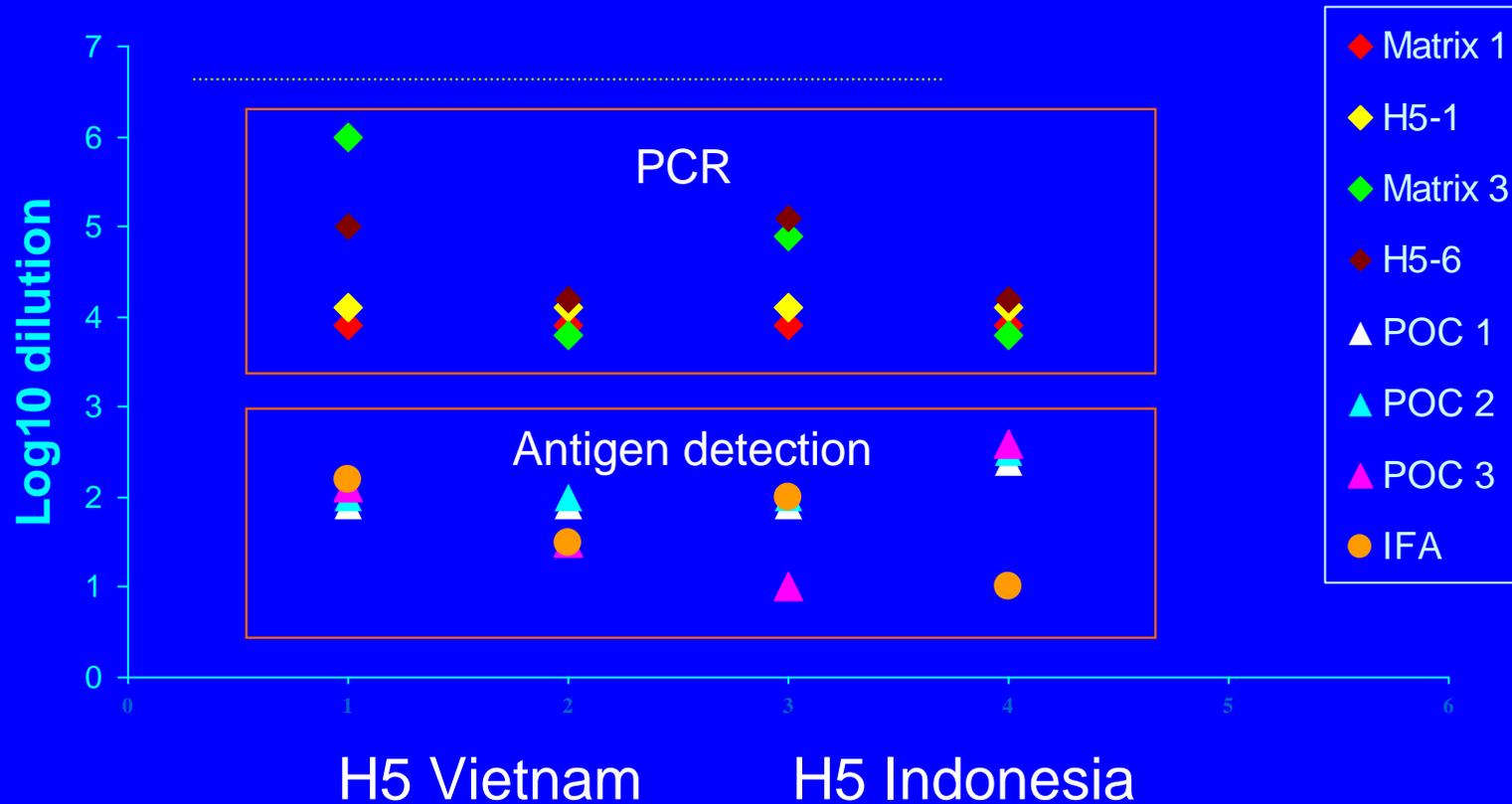
Sensitivity is type (?subtype, ?strain) dependent
Diagnostic sensitivity higher in children than adults.

Effect of specimen type on Directigen for influenza detection

- Directigen for culture positive samples
 - Kaiser *et al J Clin Virol* 1999; 14: 191-197.
 - Directigen detected
 - 75% positive nasopharyngeal washes
 - 22% throat gargles
 - 64% combined nasopharyngeal and throat swabs

Sensitivity for diagnosis depends on the type of sample collected

Sensitivity of PCR and antigen detection tests for influenza A/H5N1



H5 specific POC tests were less sensitive than the influenza A tests.
All were significantly less sensitive than PCR

QuickVue RSV: What the manufacturer says

- Nasopharyngeal aspirates:
 - Sensitivity : 99% Specificity : 92% Accuracy : 94%
- Nasal wash:
 - Sensitivity : 83% Specificity : 90% Accuracy : 87%
- Nasopharyngeal swab :
 - Sensitivity : 92% Specificity : 92% Accuracy : 92%

Sensitivity for diagnosis depends on
the type of sample collected

POC tests for RSV antigen

- Aslandezeh J et al JCM 2008 (epub)
 - 515 nasopharyngeal swabs from children
 - compared with RT-PCR
 - Sensitivities: Directigen 79.8%, DFA 94.1%
 - Specificities: Directigen 89.5%, DFA 96.8%
- Casino-Colon AE et al JCV 2003;28:169-174
 - nasopharyngeal swabs from 60 adults with proven RSV (culture, serology and/or PCR)
 - 49 PCR +/- culture positive
 - Sensitivities: DFA 26.5%, VIDAS 24.5%, Directigen 12.2%

Children have more virus than adults, so diagnostic sensitivity is better. False positives can occur.

Factors influencing performance

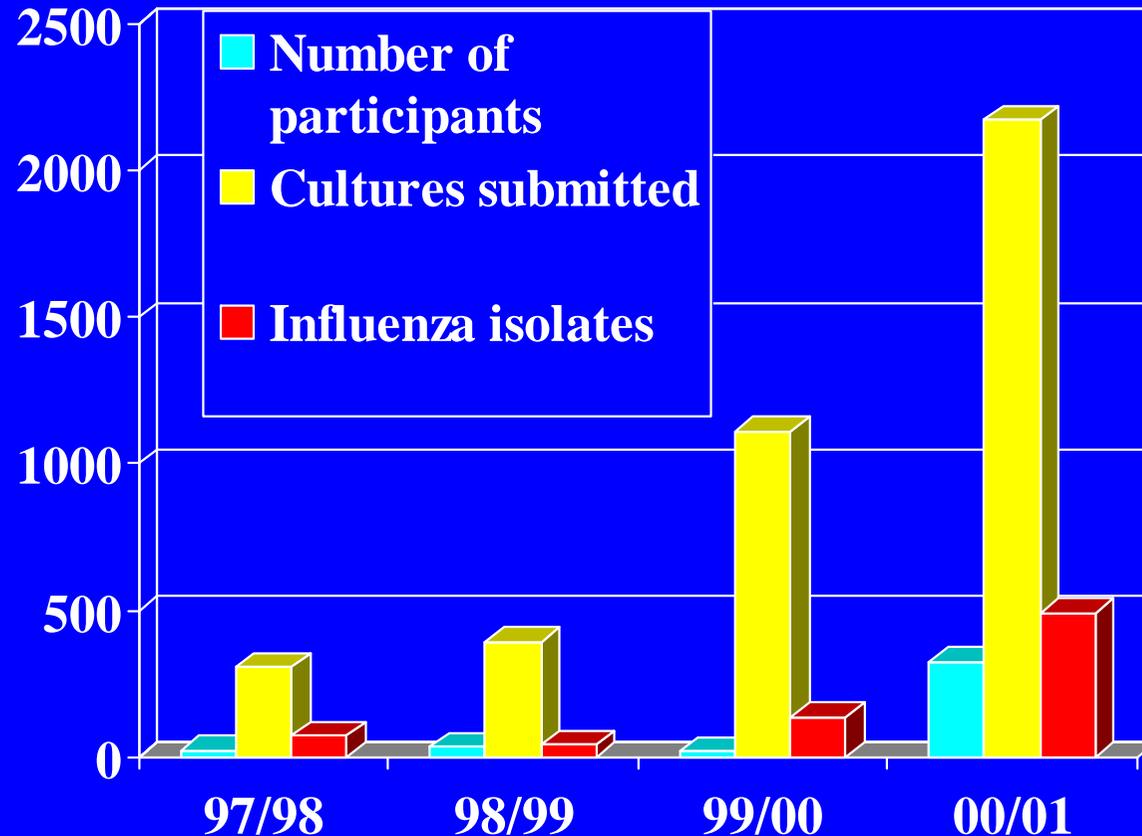
- Type of specimen
- Influenza type
- Adult versus child
- Time after onset of illness
- Operator

Potential applications of POC tests for respiratory pathogens

- Surveillance of influenza
- Individual case diagnosis
 - Case management:
 - investigations
 - antibacterial therapy
 - triaging
 - Deciding on use of antiviral therapy
- Outbreak management

Point-of-care tests for surveillance

(Effler et al. Emerg Infect Dis; 8: 23-28)



FLU OIA testing made available to doctors in Hawaii in 1999/00 and 2000/01. Tests performed at private laboratories

23% patients influenza positive by culture
OIA sens 41%, spec 88%, NPV 84%, PPV 51%.

POC tests for surveillance

- Advantages

- Increased sampling rates if access to laboratory tests is restricted

- Disadvantages

- Low positive predictive value at the beginning or end of the season may falsely suggest influenza activity when other respiratory viruses are circulating.
- Poorly performing tests will underestimate fluctuations in influenza activity
- No typing/subtyping
- Needs conventional lab test confirmation, especially early in season

Impact of point-of-care tests

Using Directigen in paediatric ED

– Noyola *et al Pediatr Infect Dis J* 2000; 19: 303-307.

– Effect of early detection of influenza

- antibiotic use reduced from 53% to 25% and average duration from 5.4 days to 3.5 days
- antiviral use increased from 1.8% to 25%

– Sharma *et al Arch Pediatr Adolesc Med* 2002; 156: 41-43.

– Impact of early vs late Dx of influenza

- ceftriaxone use reduced from 24% to 2%
- FBP reduced from 44% to 17%

POC tests for patient diagnosis

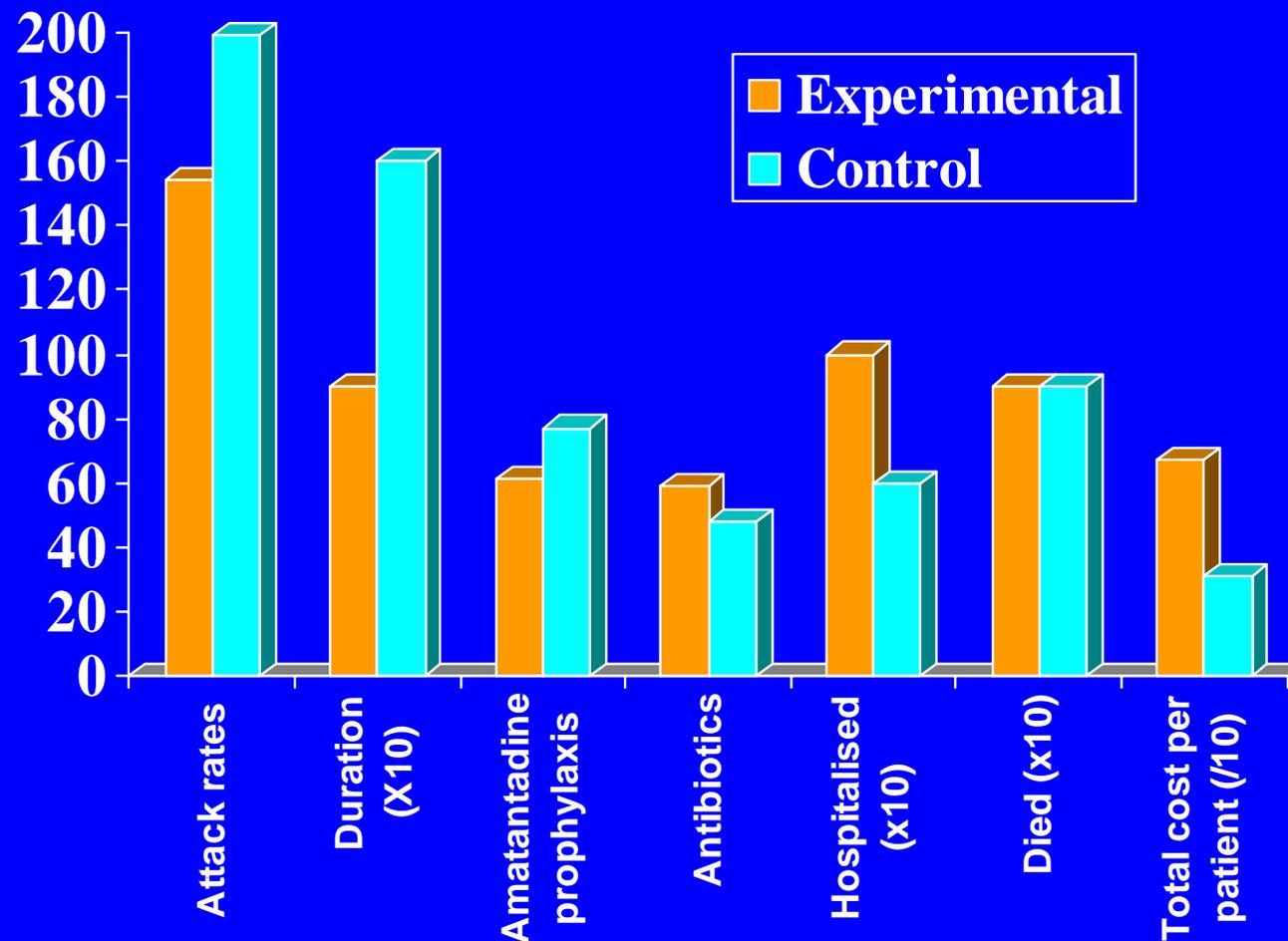
- Advantages

- Result available rapidly to assist management
- Potential to reduce unnecessary investigation and antibiotic treatment

- Disadvantages

- Misses a significant proportion of patients with influenza - problem in high risk groups
- Need to know community influenza activity
- “In use” reliability not established

Use of point of care test for influenza outbreak management in nursing homes



Church *et al.*
CID 2002; 34:
790. Compared
nursing homes
using rapid
tests with those
using culture.
All used
cohorting and
amantadine.

Point of care test for determining influenza treatment

(Sintchenko et al, *J Clin Virol* 2002; 25: 15-21)

- Decision analysis that assumed
 - Test 77% sensitive and 95% specific, clinical diagnosis correct in 70%, 5-10% adverse reactions, 25% untreated mortality in high risk groups
- If prevalence is 40% or lower, it is more cost efficient to “test and treat” rather than treat empirically
- Reducing clinical accuracy or increasing test sensitivity increases the potential value of “test and treat”.

POC tests for treatment decisions

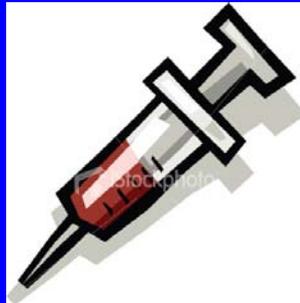
- Advantages
 - Information available at a time when it can be meaningfully used
 - More reliable than clinical diagnosis
- Disadvantages
 - Adds to the cost
 - Lack of studies on actual impact in “real life” situations
 - No mechanism for ensuring accuracy

Point of Care: At what point do we care?

Bedside



Collection Centre



Local Laboratory



Reference Laboratory



Where should we perform rapid tests?

Lab-based versus Bedside

- Lab is accredited
- Staff are trained and experienced
- Quality assurance programs in place
- Quality control of runs

- No accreditation
- No specific training requirements
- No QAP
- No QC requirements

The next steps

- Automated testing systems
- Nucleic acid detection tests
- Regulatory issues
- Funding: who pays?

There will be increasing use of point of care tests. Introduction of these tests needs to be managed properly, taking into account the limitations of the assays and the need for quality management.