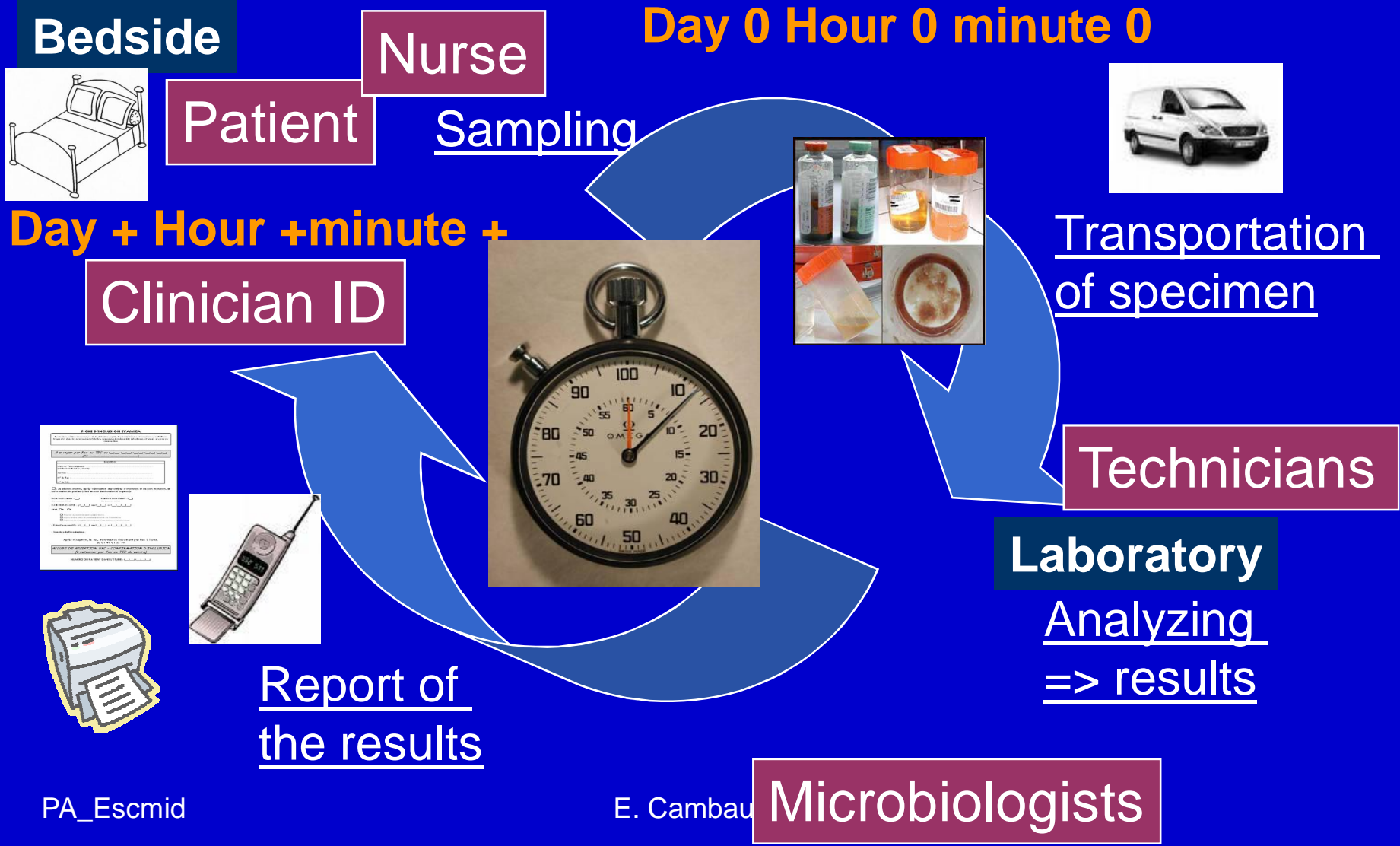


Why is the workflow in Clinical
Microbiology so slow?
Can we get it quicker?

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Workflow in Clinical Microbiology



Why is the workflow in Clinical Microbiology so slow?

Can we get it quicker?

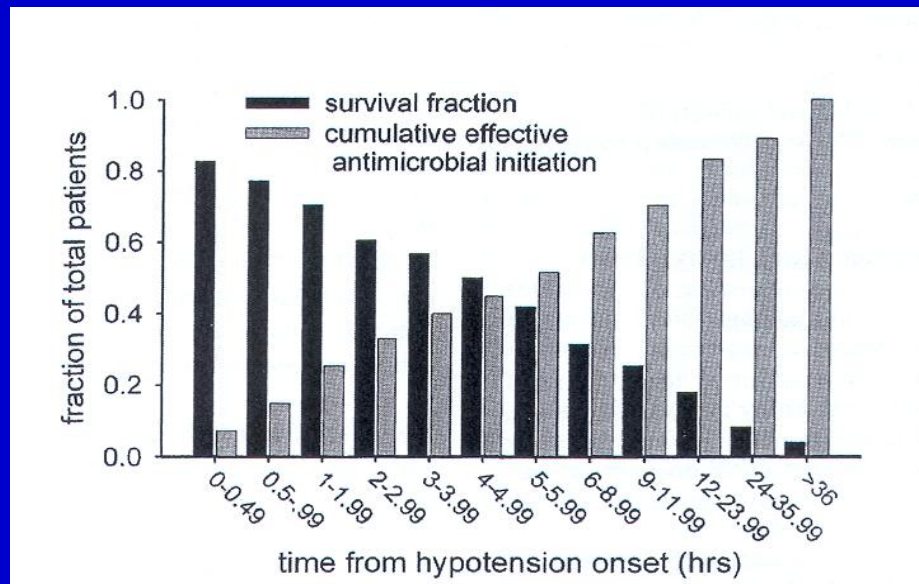
Two main limiting factors

- Analytical: Bacterial growth
- Pre and post analytical :
 - Logistic and organization: transportation of specimen, softwares and computers
 - Place: hospital or out, public vs. private
 - Human beings : nurse, clinicians, technicians, and micro biologists (secretaries, unqualified employees...)

Why getting quicker?

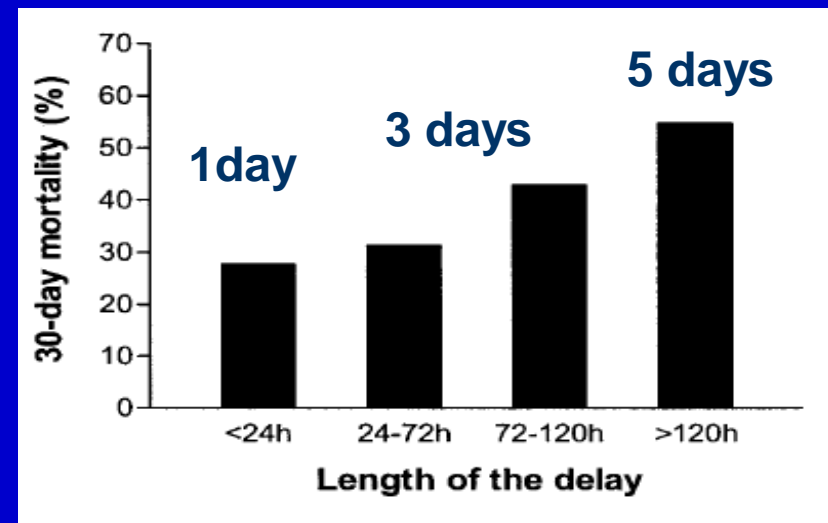
**“The GOLDEN hours”
link between antibiotic treatment timing and
mortality**

in septic shock



Kumar CCM 2006, 34,1589

in *P.aeruginosa* bacteremia



Kang , CID 2003

Why getting quicker?

Two main reasons



Patient :

- Adequate antibiotherapy (=adequate diagnosis) decreases infection related mortality
- length of hospital stay or prescription of unnecessary antibiotics (increase in side effects)



Hospital, laboratory, social insurances costs

- because of increase in hospitalization days and investigations

How to speed up

- (1) Bring the patient close to the lab (private out lab)
- Bring the lab close to the patient (point of care)
- Rapid sampling (2 first blood cultures in 15 min)

Day + Hour +minute +

Clinician ID

Bedside

Patient

Day 0 Hour 0 minute 0

Sampling

Technicians

Laboratory

Analyzing

=> results

Report of
the results

Microbiologists



PA_Escmid

E. Cambau

How to speed up

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Report of the results



Laboratory
Analyzing
=> results

=> speed the pre-
and the post-analytical

Microbiologists

How to slow down ?

Time to incubation

- = Time between sampling and culturing
- mean of 3.5 hours for blood culture from veinipuncture to incubation in the automate
- Varies depending on organization, distance from ward to laboratory, open hours, etc....
 - Night vs. Day : increase of 5 hours
- Increases the time to positive result from 1 to 3.5 days for blood culture

Bengtsson 1998, Savinelli 2004, Akan 2006, Kobayashi 2004, Saito 2004

(2) Speed the growth detection

Limiting factors

- Type of bacteria (growth rate) : mean time 10h - 20h in blood culture
- Number of bacteria in the specimen
 - from 0.1/ml to $>10^5$ /ml
 - 10-fold => 10% decrease
- Presence of antibiotics +++
- Bacterial physiology state

TABLE 4. Mean times to detection of clinically important isolates from adequately filled bottles by the VTI and 3D blood culture systems

Microorganism (no. of isolates or strains)	Mean time to detection (h) by:	
	VTI	3D
Gram-positive cocci		
<i>S. aureus</i> (43)	17.6	19.1
Coagulase-negative staphylococci (36)	21.6	21.0
<i>Streptococcus</i> and <i>Enterococcus</i> spp. ^a (60)	15.7	17.9
Gram-negative bacilli		
<i>Enterobacteriaceae</i> ^b (95)	15.0	15.9
Nonfermenters ^c (20)	14.9	16.2
Anaerobic bacteria ^d (11)	25.3	23.9
Yeasts ^e (23)	35.8	37.5
All microorganisms (288)	18.4	19.6

Mtb Medium	specimen	
	Smear +	Smear -
Solid	14-21	21-42
Liquid*	5-10	10-28

(3) Time saved by automation?

	Manual	Automate
Registration	by hand	Barcode Computer prescribed
Reading of cultures	At most 2 times a day	Every 10 min or continuous
Detection of growth	macroscopic	CO2 production or O2 consumption
Report	by hand	Connection to laboratory computers
Time to detection	24h – 36h	10h-20h



E. Cambau



Mirrett 2003; Cockerill 1997

(4) After the detection of positive blood culture

- Gram staining
- Identification
- Susceptibility testing
- Molecular biology

As quick
as possible

**=> Directly from
the positive
blood culture
bottle is quicker
than from a 18h-
subculture**

Phenotypic susceptibility testing directly from positive blood cultures

example of gram-negative bacilli

TABLE 5. Synopsis of results of recently published evaluations of direct ID and susceptibility testing of GNRs from positive BCs

Authors (reference)	Yr of publication	Testing purpose ^a	No. of strains included	% Correct identification	% Strains with:			Method
					Very major error	Major error	Minor error	
Putnam et al. (9)	1997	SUS	50		0.3	0.9	6.4	BACTEC system with VITEK 1 system
Waites et al. (12, 13)	1998	ID, SUS	133	96/72 ^b	2.7/8.1 ^b	1.4/0.7 ^b	ND ^c	BacT/Alert system with MicroScan system
Steinbrückner et al. ^d	2001	ID, SUS	65	82	0.1	0.0	2.3	BacT/Alert system with VITEK 2 system
Hansen et al. (4)	2002	ID, SUS	169	75	0.0	0.7	0.4	BACTEC system with VITEK 1 system
Fontanals et al. (3)	2002	ID, SUS	118	98.3	0.1	0.3	2.2	BacT/Alert system with Wider system
Ling et al. (5)	2003	ID, SUS	118	82.2	0.2	0.4	1.9	BacT/Alert system with VITEK 2 system
Present study	2004	ID, SUS	309	92.9	0.1	0.1	0.8	BACTEC system with PHX system

^a SUS, susceptibility.

^b Data for overnight panels/data for rapid panels.

^c ND, no data.

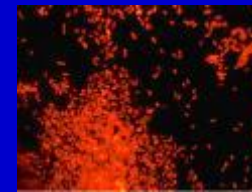
^d Jahrestagung Dtsch. Ges. Hyg. Mikrobiol., poster P16, 2001.

Review by Funke, JCM 2004

=> Less than 1% major errors comparing with susceptibility testing performed on subculture

(5) Circumventing the bacterial growth limiting factor

- Amplification of specific bacterial DNA
- Identification
 - DNA probe
 - FISH
 - mass spectrometer
- Detection of mutations conferring antibiotic resistance



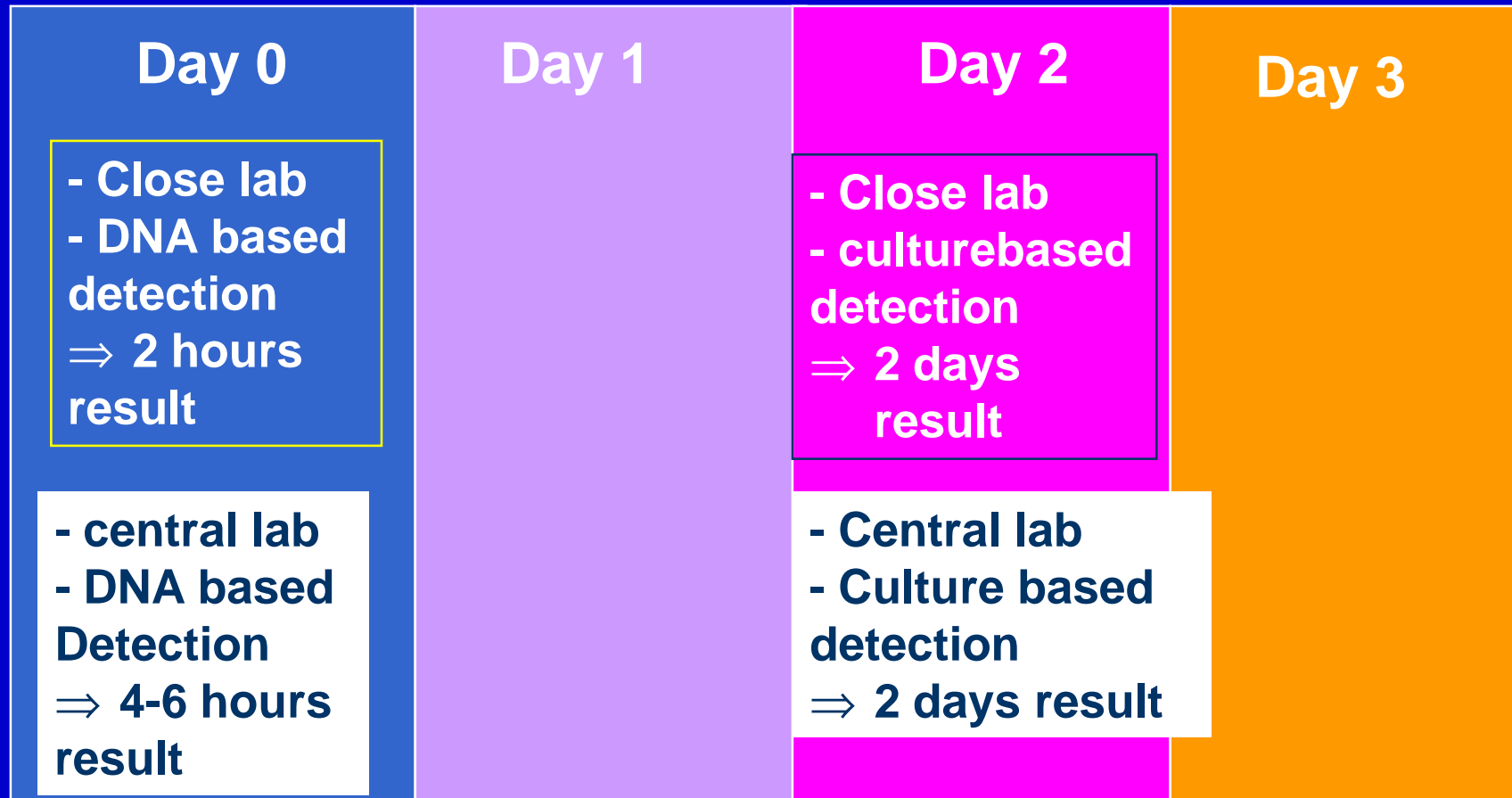
PA_Escmid => not enough industrial development E. Cambau

1	Conjugate Control (CC)
2	Universal Control (UC)
3	<i>M. tuberculosis</i> complex (TUB)
4	<i>rpoB</i> Uni
5	<i>rpoB</i> WT 1
6	<i>rpoB</i> WT 2
7	<i>rpoB</i> WT 3
8	<i>rpoB</i> WT 4
9	<i>rpoB</i> WT 5
10	<i>rpoB</i> MUT D516V
11	<i>rpoB</i> MUT H526Y
12	<i>rpoB</i> MUT H526D
13	<i>rpoB</i> MUT S531L
14	<i>katG</i> Uni
15	<i>katG</i> WT
16	<i>katG</i> MUT 1
17	<i>katG</i> MUT 2
	colored marker

How to slow down Time to report of positive and negative results

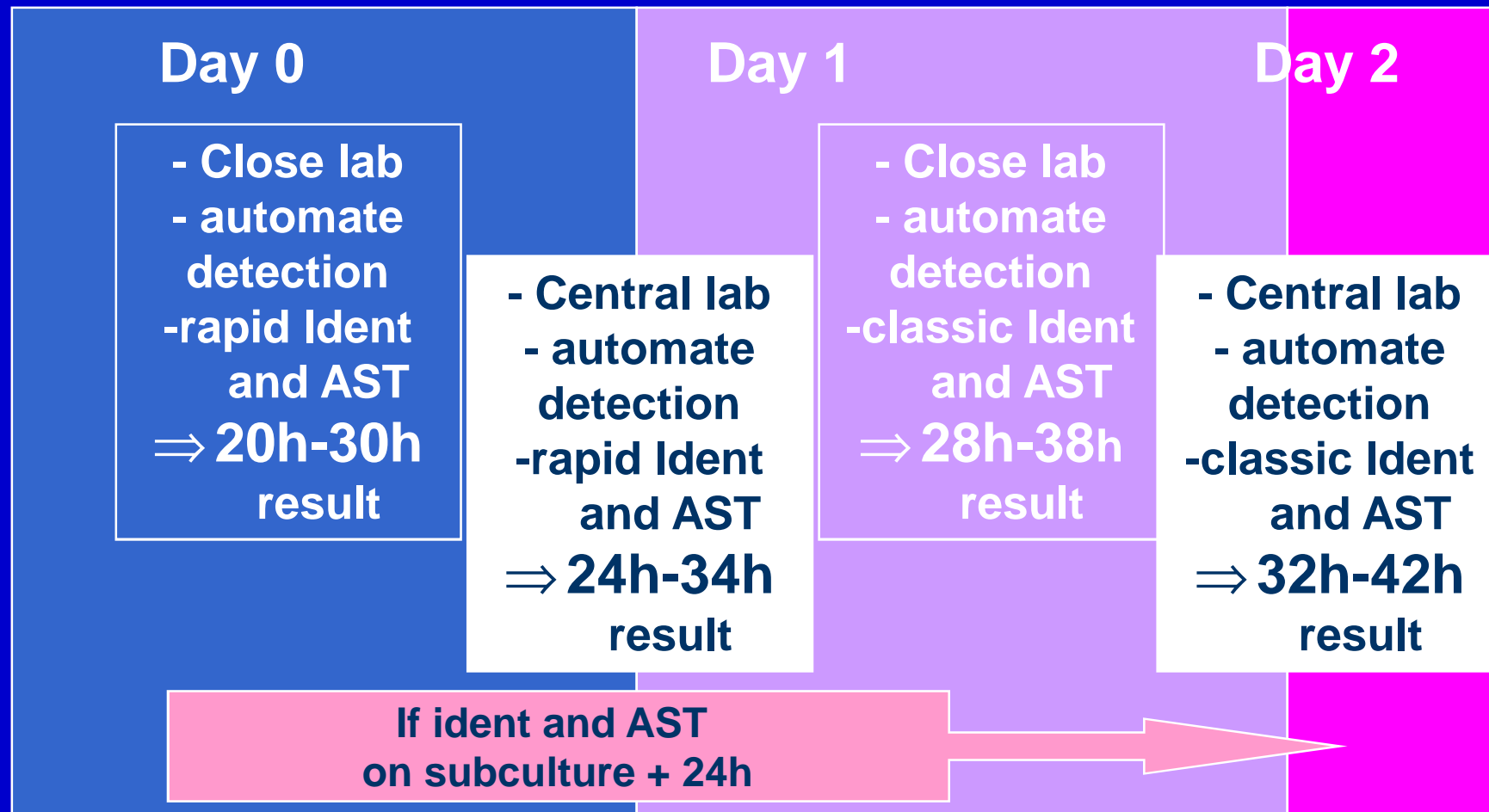
- depends on the
 - When you get the results
 - Presence in the lab of technicians and biologists
 - How it is reported (oral vs written vs computer)
 - Presence of clinician in the ward to look at the result and modify the treatment

Continuous workflow ex. detection of MRSA



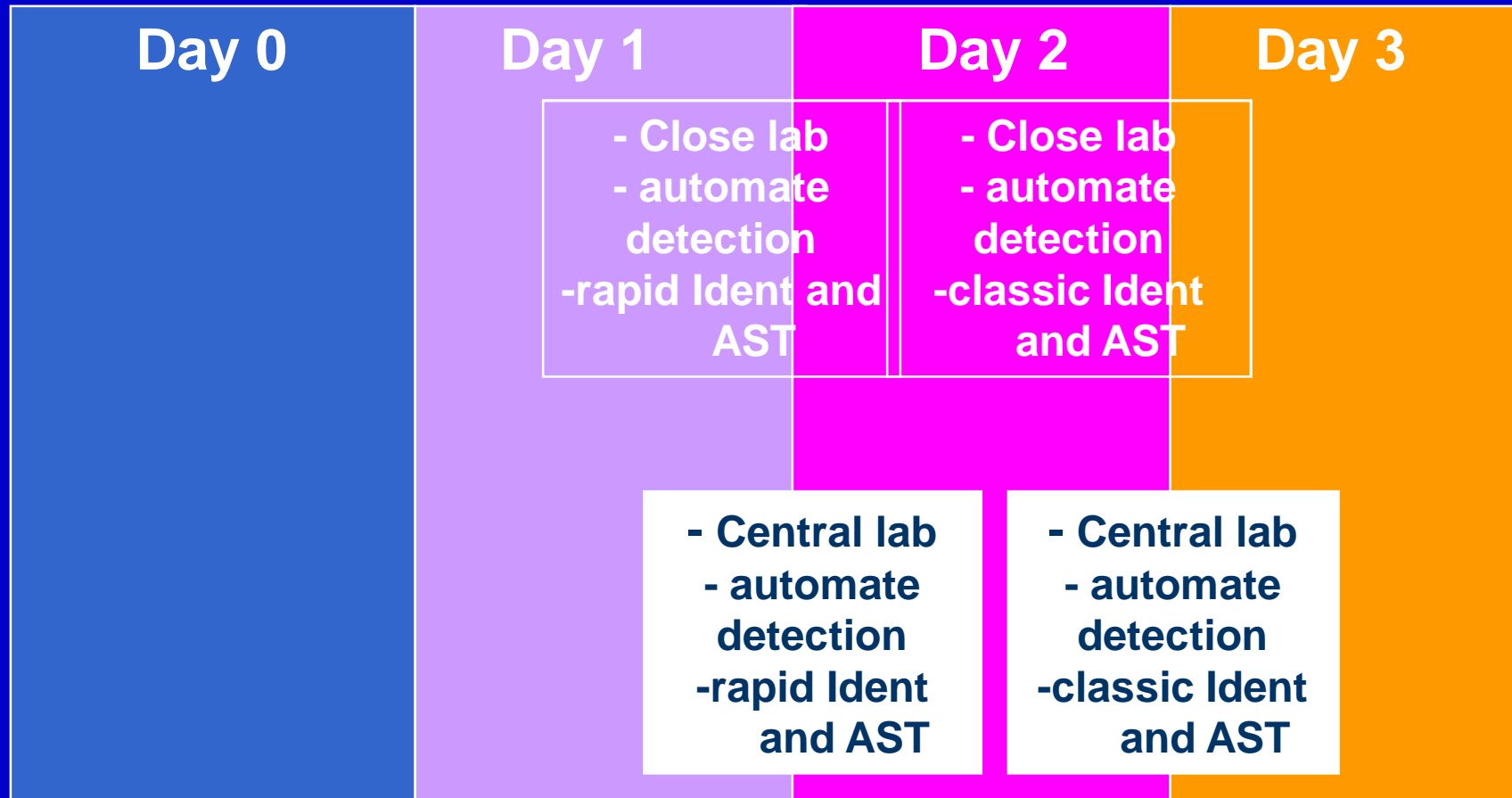
⇒ **technology makes the difference**

Continuous (day and night) workflow ex. blood culture



PA_Escort
Close lab or Rapid ID and AST makes the difference

Discontinuous (day only) workflow ex. blood culture



=> The presence of technicians or microbiologists makes the difference

PA_Escmid

E. Cambau

Getting the workflow quicker is
worthwhile

It resulted from
adequate automation and investment in the
most rapid technology
(industrial new proposals are mandatory)

+

24h-involvement and commitment
of microbiologists and technicians

Parameters for shortening or slowing the workflow in clinical microbiology

- Quantity of bacteria
- Technology for detection
- (Automation)
- Distance from lab to patient
- Hours of opening / hours of sampling