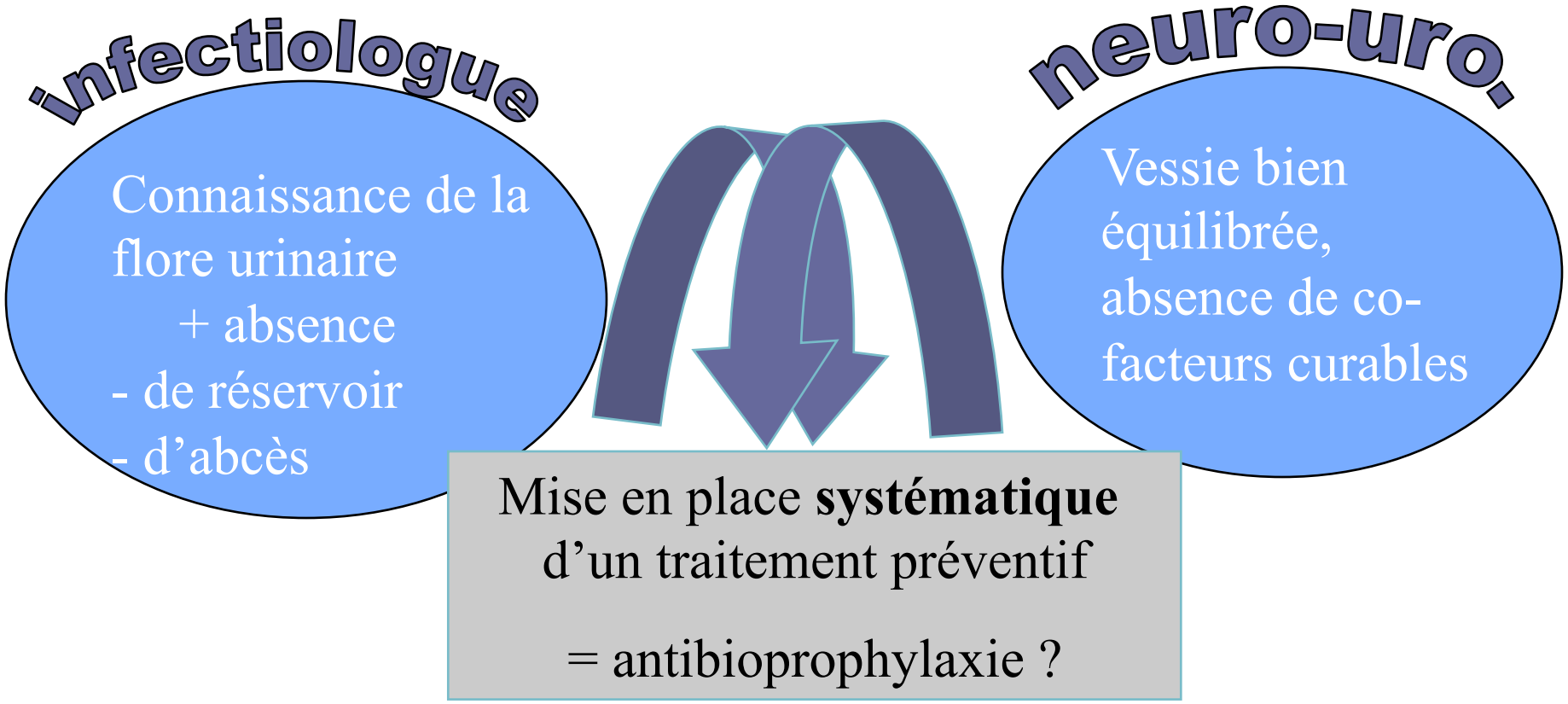
Antibiocycle

A.EVEN et A.DIHN
Hôpital Raymond Poincaré, Garches

Infections urinaires à répétition chez le neurologique



Bilan préalable

- S'assurer qu'il s'agit d'infections urinaires vraies (≠ colonisations)
- Catalogue mictionnel
- Bilan urodynamique
- Imagerie de l'appareil urinaire (écho, TDM)
- +/- uréthrocystographie rétrograde si infections fébriles

ECBU hebdomadaires avec antibiogramme complet ++

pendant 6 semaines (6 ECBU)

Antibiothérapie en continu

Pas de preuve suffisante pour la recommander :

- peu de bénéfice prouvé en terme d' infection clinique
- effets II, allergies…
- risque écologique: émergence de BMR

Morton SC, Arch Phys Med Rehabil 2002
BS, Urinary catheter policies Cochrane Database. 2005

Antibiothérapie en continu

Pas de preuve suffisante pour la recommander : effets II, allergie…

(19 études contrôlées, 2 méta analyses)

(Morton SC, Arch Phys Med Rehabil 2002;83:129-38)

Peu de bénéfice prouvé en terme d'infection clinique

Risque écologique: (BMR X 2) sous Ciprofloxacine

(Elden, Arch Phys Med Rehabil, 1997;78:468-70)

NON !

Niel-Weise BS, Urinary catheter policies Cochrane Database. 2005 Jan 25;(1):CD004201.
Huertas, Cochrane library, 2008

Continuous low-dose antibiotic prophylaxis for adults with repeated urinary tract infections (AnTIC): a randomised, open-label trial

*Holly Fisher, Yemi Oluboyede, Thomas Chadwick, Mohamed Abdel-Fattah, Catherine Brennand, Mandy Fader, Simon Harrison, Paul Hilton, James Larcombe, Paul Little, Doreen McClurg, Elaine McColl, James N'Dow, Laura Ternent, Nikesh Thiruchelvam, Anthony Timoney, Luke Vale, Katherine Walton, Alexander von Wilamowitz-Moellendorff, Jennifer Wilkinson, Ruth Wood, Robert Pickard**

361 patients sous AS
40% neuro

	Prophylaxis group (n=181)*	No prophylaxis group (n=180)*	Incidence rate ratio (95% CI)	p value
Symptomatic, antibiotic-treated urinary tract infections†				
All eligible participants	1·3 (1·1–1·6)	2·6 (2·3–2·9)	0·52 (0·44–0·61)	<0·0001
<4 infections at baseline	0·8 (0·6–1·1)	1·7 (1·4–2·2)	0·46 (0·34–0·64)	0·45‡
≥4 infections at baseline	1·7 (1·3–2·0)	3·1 (2·7–3·6)	0·54 (0·45–0·64)	··
Microbiologically confirmed urinary tract infections§				
All eligible participants	0·74 (0·58–0·94)	1·5 (1·3–1·8)	0·49 (0·39–0·60)	<0·0001
<4 infections at baseline	0·32 (0·18–0·57)	1·2 (0·9–1·5)	0·28 (0·18,0·45)	0·01‡
≥4 infections at baseline	0·99 (0·77–1·3)	1·7 (1·4–2·1)	0·57 (0·45–0·72)	··
Febrile urinary tract infections§				
All eligible participants	0·11 (0·06–0·21)	0·16 (0·10–0·25)	0·71 (0·40–1·26)	0·24
<4 infections at baseline	0·07 (0·03–0·17)	0·12 (0·06–0·23)	0·62 (0·20–1·90)	0·79‡
≥4 infections at baseline	0·14 (0·06–0·30)	0·19 (0·11–0·32)	0·74 (0·38–1·45)	··
Asymptomatic bacteriuria§				
All eligible participants	1·4 (1·2–1·6)	1·6 (1·4–1·9)	0·88 (0·74–1·04)	0·14
<4 infections at baseline	1·5 (1·2–2·0)	2·0 (1·6–2·5)	0·77 (0·60–1·00)	0·18‡
≥4 infections at baseline	1·3 (1·1–1·6)	1·4 (1·1–1·6)	0·98 (0·77–1·23)	··

Continuous low-dose antibiotic prophylaxis for adults with repeated urinary tract infections (AnTIC): a randomised, open-label trial

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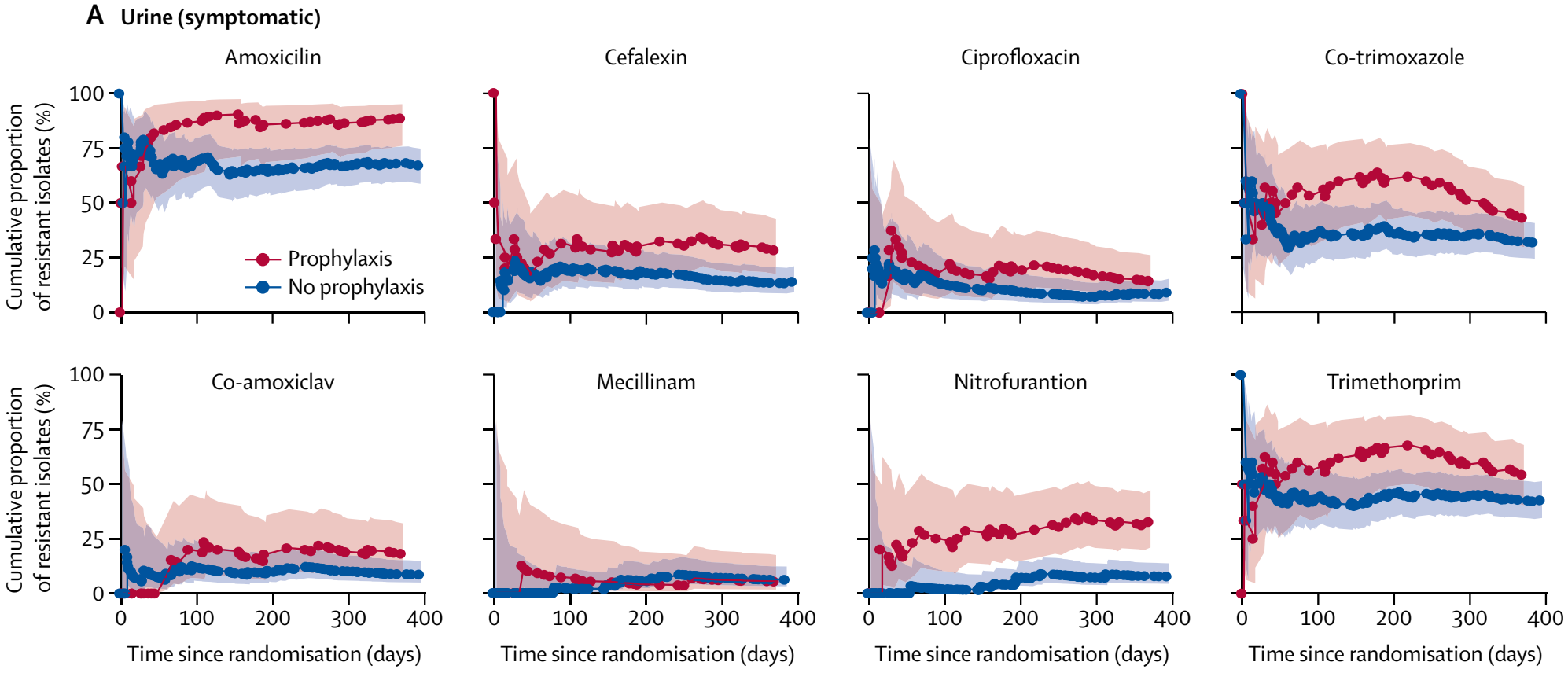
Risque écologique++



Antibiocycle « WOCA »

- Principe :
  - 1 prise unique hebdomadaire alternée d'un antibiotique A ou B parmi cefixime, amoxicilline, fosfomycine, cotrimoxazole, furadantine
- Objectif principal :
  - éviter IUS chez blessés médullaires sous sondages intermittents,
- Objectifs secondaires :
  - tolérance, consommation ATB, BMR en anal (entérobactéries BLSE)

Salomon J. et al. JAC 2006

Journal of Antimicrobial Chemotherapy (2006) 57, 784–788
doi:10.1093/jac/dkl010
Advance Access publication 10 February 2006

JAC

Prevention of urinary tract infection in spinal cord-injured patients: safety and efficacy of a weekly oral cyclic antibiotic (WOCA) programme with a 2 year follow-up—an observational prospective study

Jérôme Salomon[1], Pierre Denys[2], Corinne Merle[1], Emmanuel Chartier-Kastler[2], Christian Perronne[1], Jean-Louis Gaillard[3] and Louis Bernard[1]*

- Étude prospective, 38 patients, suivi 2 ans
- Blessés médullaires (hors grossesse), IU à répétition
- 22 hommes / 16 femmes
- Age : 46 ans
- 32 paraplégiques, 6 tétraplégiques
- Mode mictionnel : sondage intermittent sur vessie neurologique
- Historique : 9,4 IUS / patient an
  0.75 IUF / patient an
- 150 PNA, 40 prostatites, 7 orchi-épididymites,
- 50 hospitalisations

Résultats

Variables	Avant	Après	p
IUS	9.4	1.84	0.0002
IUF	0.74	0.31	0.04
Orchite	7	0	
Pyélonéphrite	150	13	
Prostatite	40	6	
Hospit/an	0.23	0.09	0.0012
Jour hospit	3.97	1.18	<0.0001
Jours ATB	111	56	0.01
Large spectre	77	12	<0.0001
ECBU +	98.4%	31.8%	<0.0001
% BMR	52	6	<0.0001
Patients BMR	6/38	2/38	

Salomon J. et al. JAC 2006

In real life !

Suivi > 2 ans (moy 63 mois)
50 patients

Table 1 Characteristics of patient included in the weekly oral cycling antibiotics program.

Male	n = 30 (60%)
Female	n = 20 (40%)
Sex ratio	1.5
Age (years)	
Mean (±SD)	51 ± 13.5
Min	20
Max	81
Injuries	
Paraplegia	n = 33 (66%)
Tetraplegia	n = 6 (12%)
Multiple sclerosis	n = 4 (8%)
Others	n = 6 (12%)
No data	n = 1 (2%)
Level of SCI	
Cervical	n = 7 (14%)
Thoracic	n = 26 (52%)
Lumbar	n = 5 (10%)
No data	n = 12 (24%)
Date of injury (years)	
Mean ± SD	19.4 ± 14.3
Min	2
Max	58
History of injury	
Accidental cause	n = 27 (54%)
Infectious cause	n = 2 (4%)
Congenital defects	n = 5 (10%)
Inflammatory/Auto-immune cause (Behcet ...)	n = 4 (8%)
Mechanical cord compression (neoplasia, arthrosis, lipoma)	n = 6 (12%)
Brain injury	n = 1 (2%)
No data	n = 5 (10%)
Immunosuppression	
Yes	n = 6 (12%)
No	n = 44 (88%)
No data	n = 0
Voiding activity	
Self-catheterization	n = 44 (88%)
Hetero-catheterization	n = 2 (4%)
Endoprothesis	n = 2 (4%)
Bladder plasty	n = 0
Indwelling catheter	n = 0
Reflex urination	n = 2 (4%)
Others	n = 2 (4%)
No data	n = 1 (2%)
Frequency of urination (/day)	
Mean ± SD	6 ± 1.7
Min	4
Max	15
Characteristics of the bladder	
Hyperactive	n = 14 (28%)
Non-contractile	n = 18 (36%)
Others	n = 2 (4%)
No data	n = 16 (32%)

Table 2 Frequency of urinary traction infection, hospitalization, antibioticuse and multidrug resistant organisms (MDRO) organism colonization before and under weekly oral cycling antibiotics (WOCA).

	Prior WOCA	Under WOCA	*p*
Urinary tract infection (UTI) per patient per year:			
Cystitis	9.45	1.57	0.0001
Febrile UTI	5.25	0.18	0.0001
Hospitalization and antibiotic use:			
Hospitalizations per patient per year	0.86	0.02	0.002
Total hospital days per patient per year	5.37	0.16	0.001
Total days of curative antibiotic treatment per patient per year	92.83	34.5	<0.0001
MDR colonization:			
Percentage of positive urine sample cultures	86%	57%	<0.0001
MDRO-colonized patients	9	4	NS

C. Poirier et al. J Infection 2015

Antibiocycle

*Aurélien Dinh, Benjamin Davido, Clara Duran, Frédérique Bouchand, Louis Bernard
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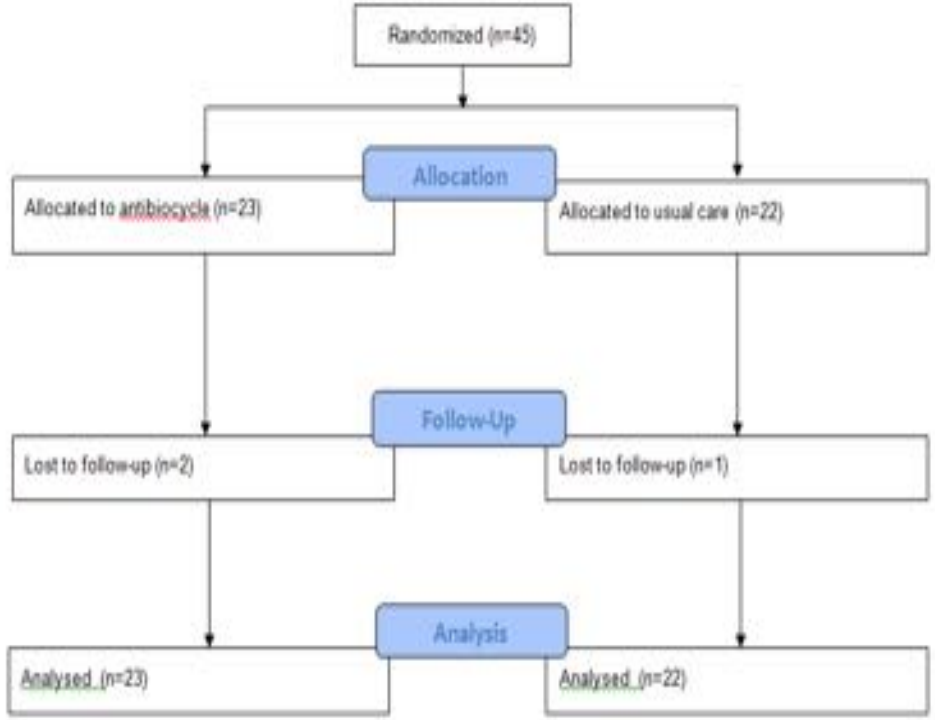
Thus, we believe that, when antibiotic prophylaxis is required, a weekly intermittent high dose of cyclic antibiotic treatment is effective and does not engender emergence of resistance. These results should soon be confirmed by the PACHIU trial (NCT01388413).

Thelancet.com/infection Vol 18 Oct 2018

PACHIU



Variable	WOCA N = 23	Standard treatment N = 22
Sex (n, %)		
Female	7 (30.4%)	8 (36.4%)
Male	16 (69.6%)	14 (63.6%)
Age (year, median, IQR)	48.7 [41.5 ; 60.0]	49.6 [34.7 ; 57.5]
Number of UTI per year (median, IQR)	12.0 [6.5; 12.0]	9.5 [6.0; 11.8]
Number of febrile UTI per year (median, IQR)	0.0 [0.0; 2.0]	2.0 [0.0; 3.0]
Orchitis	1 (4.3%)	1 (4.5%)
Epididymitis	2 (8.7%)	0 (0%)
Prostatitis	6 (26.1%)	3 (13.6%)
Pyelonephritis	7 (30.4%)	13 (59.1%)

Essai randomisé, suivi 6 mois.

PACHIU

Variables	WOCA	Standard treatment	P-value
Number of UTIs (median, IQR)	1.0 [0.5-2.5]	2.5 [1.2-4.0]	0.024
Febrile UTI (n, %)	0 (0%)	9 (45.0%)	<0.001
N Hospitalizations	3 (13.6%)	6 (28.6%)	0.281
N antibiotic (median, IQR)	0.0 [0.0-2.0]	3.0 [2.0-5.0]	0.004

BMR en cours d'analyse…

Antibiocycle et grossesse

Control Cross-sectional Study Evaluating an Antibiotic Prevention Strategy in 30 Pregnancies Under Clean Intermittent Self-catheterization and Review of Literature.

[Antibioprophylaxy and urological management of women with spinal cord injury during pregnancy].

[Article in French]

- Diminution significative des infections pendant la grossesse

Take home messages

- Antibiocycle:
  - Indiqué après éviction des facteurs de risque d'infections urinaires à répétition
  - Efficace sur les infections urinaires fébriles ou non fébriles
  - Pas d'augmentation de résistances bactériennes
  - Indication également pendant la grossesse chez les patientes BM en AS

- A discuter:
  - Les modalités d'arrêt (quand? brutal ou progressif?)

Je vous remercie pour votre attention.

Questions

- Furadantine>> OK
- Selexid/pivecillinam ?
- Forte dose : fosf 2 sachets/furadantine 2 gelX3/j/oroken 1cpX3 ?
- 2 prises par semaine
- Quand arrêter ? Queqlues années ? Diminuer les doses ?
- Pour qui ? Tout le monde !