during hospitalisation: being male (odds ratio [OR], 2.42, Wald test $P = 0.03$); increased Charlson score (OR, 1.50 for each additional point between 3 and 13; $P < 0.001$); decreased systolic blood pressure (OR, 6.71 for systolic blood pressure < 100 mmHg; $P = 0.004$); abnormal heart rate (< 60 beats/min or > 100 beats/min) (OR, 3.63; $P = 0.003$); increased RR (OR, 1.81 for each additional 5 breaths/min between 14 and 44; $P < 0.001$); abnormal blood sodium level (< 137 mmol/L or > 143 mmol/L) (OR, 2.82; $P = 0.01$) and raised C-reactive protein level (OR, 2.67 for C-reactive protein level > 45 mg/L; $P = 0.02$).

After multivariate logistic regression analysis with stepwise backward elimination, the only remaining factors that were significant predictors of death during hospitalisation were Charlson score (OR, 1.53 for each additional point between 3 and 13; $P < 0.001$) and RR (OR, 1.83 for each additional 5 breaths/min between 14 and 44 breaths/min; $P < 0.001$).

RR on admission was associated with an area under the ROC (receiver operating characteristic) curve of 0.73 (95% CI, 0.64–0.82) for the prediction of death during hospitalisation. An RR of ⩾ 20 breaths/min had a sensitivity of 97% (95% CI, 80%–100%), a specificity of 28% (95% CI, 21%–35%) and a negative likelihood ratio of 0.12 (95% CI, 0.02–0.82) for prediction of death during hospitalisation. Only one patient (admitted for stroke) with an RR of < 20 breaths/min at admission died in hospital. Higher RR cut-off values increased specificity but reduced sensitivity. For instance, an RR of ⩾ 30 breaths/min had a specificity of 90% (95% CI, 84%–94%), but a sensitivity of 38% (95% CI, 21%–58%), leading to a positive likelihood ratio of 3.68 (95% CI, 1.93–7.04) for prediction of death during hospitalisation.

In conclusion, besides comorbidity (Charlson score), RR was the most useful predictor of death in acutely hospitalised patients aged over 75 years. Our results extend the evidence base promoting regular documentation of RR in acute-care departments.[1]

Olivier Steichen, Fellow[1]
Gilles Grateau, Professor and Head[1]
Eric Bouvard, Head[2]
1 Department of Internal Medicine, Hôpital Tenon, AP-HP, Paris, France.
2 Department of Geriatrics, Hôpital Tenon, AP-HP, Paris, France.
olivier.steichen@tnn.aphp.fr

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Simon C Gandevia and David K McKenzie

To the Editor: The concept that respiratory rate (RR) is a key vital sign is hardly new,[1] but it is being re-emphasised.[2,3] The recent article by Cretikos et al[3] highlights the diagnostic relevance of a raised RR for serious adverse events. The authors make sensible recommendations regarding the need to educate hospital staff about the importance of measuring patients' RR.

However, they do not specify how this rate should be measured. Indeed, most textbooks of general medicine, and even respiratory medicine, fail to provide guidance on this or to define an abnormal rate. A widely used book on clinical examination[4] suggests measuring RR while feeling the pulse, and quotes a normal (adult) resting range of 16–25 breaths/min, but no source for this information is provided.

There are few reports of true normal resting RR measurements obtained by covert observation. Respiratory physiologists have long known that RR commonly increases and becomes more regular as soon as a subject becomes aware of the measurement. This is especially so if a mouthpiece is in place. Rates as low as 8 breaths/min may be seen at rest, and the normal adult range quoted by physiologists is 11–14 breaths/min.[5] Bradypnoea is usually defined as a rate less than 8 breaths/min and tachypnoea as a rate greater than 18–20 breaths/min.

There is no gold standard method for accurate measurement of RR in clinical practice. Of course, when patients are being monitored, particularly with a nasal cannula, it should be easy to obtain the rate. Oximetry is not a surrogate measure of RR, although it is often easier to record. Inductance bands around the chest provide a simple non-invasive way to measure RR. In addition to the absolute rate, an irregular and erratic rate is of concern.

In settings in which formal monitoring is not being conducted, RR is the one "vital" sign that must be assessed when the patient is resting quietly, unaware of its measurement, and not conversing with staff. Duplicate measurements should be made over an interval of at least 1 minute. An RR of over 20 breaths/min, particularly if irregular, is noteworthy. Tachypnoea is intimately linked with the sensation of breathlessness, and hence the patient's respiratory sensations should be assessed. In some patients with a normal RR at rest, marked tachypnoea may be precipitated by mild exertion, such as walking a few paces.

Simon C Gandevia, Deputy Director[1]
David K McKenzie, Head[2]
1 Prince of Wales Medical Research Institute, Sydney, NSW.
2 Department of Respiratory and Sleep Medicine, Prince of Wales Hospital, Sydney, NSW.
S.Gandevia@unsw.edu.au

1 Lenfant C. Time-dependent variations of pulmonary gas exchange in normal man at rest. *J Appl Physiol* 1967; 22: 675-684.
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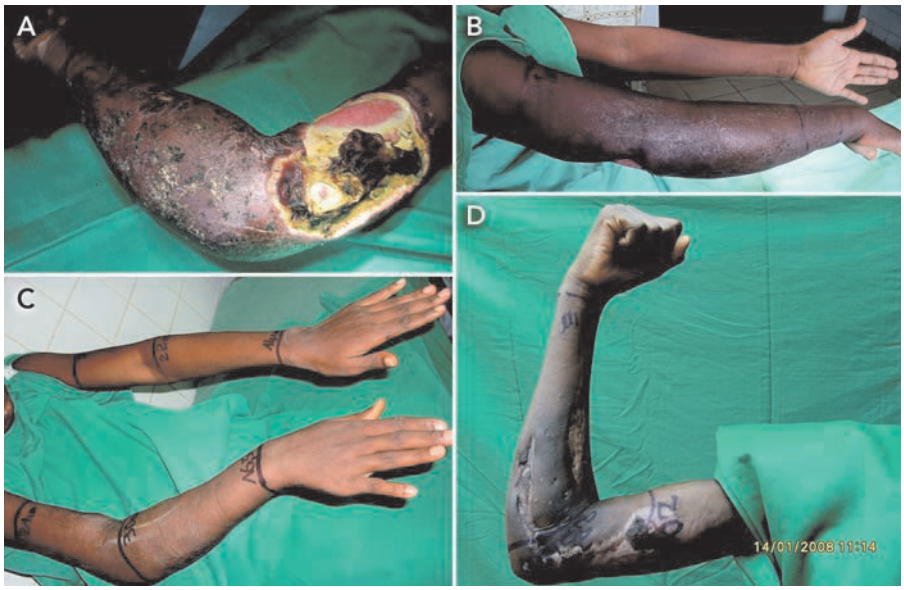
Management of *Mycobacterium ulcerans* infection in a pregnant woman in Benin using rifampicin and clarithromycin

Ange D Dossou, Ghislain E Sopoh, Christian R Johnson, Yves T Barogui, Dissou Affolabi, Sévérin Y Anagonou, Théophile Zohoun, Françoise Portaels and Kingsley Asiedu

To the Editor: Buruli ulcer, caused by the bacterium *Mycobacterium ulcerans*, leads to the destruction of skin and sometimes bone. It has been reported in many tropical countries in Africa and in some temperate regions of Australia, Japan and China.[1] In 2004, the World Health Organization recommended treatment with the combination of oral rifampicin and intramuscular streptomycin (or amikacin) for 8 weeks.[2,3] In-vitro studies and new data from mouse models suggest that combinations of rifampicin with clarithromycin, rifampicin with moxifloxacin, or clarithromycin with moxifloxacin may be as effective as rifampicin and streptomycin.[4,5]

In June 2007, a woman who was 6-months pregnant with her first child and had a 7-month history of Buruli ulcer on her right upper limb (Box 1, A) was admitted to the Buruli ulcer treatment centre in Allada,

1 Serial views of Buruli ulcer in a woman treated with rifampicin and clarithromycin



A: At presentation. B: After 4 weeks' antibiotic treatment. C: On completion of antibiotic treatment (8 weeks). D: At hospital discharge after skin grafting, showing full movement of the elbow joint (23 weeks). ◆

2 Clinical response to treatment

	Week after treatment start			
	0	4	8	23
Limb circumference (cm)				
At wrist				
Affected limb	21	17.5	16.5	15
Unaffected limb	14	14	14	14
% difference	50%	25%	18%	7%
At mid-arm				
Affected limb	36	33	30	25
Unaffected limb	22	22	22	22
% difference	64%	50%	36%	14%
At elbow				
Affected limb	34	21	21	21
Unaffected limb	23	23	23	23
% difference	48%	– 9%	– 9%	– 9%
Lesion dimensions				
Diameter (cm)*	30.3	23.8	22.5	20.3
Area				
Estimate (cm^2)	722	446	397	325
% reduction	—	38%	45%	55%

* Median diameter. ◆

Benin. She was otherwise in good health, and the fetal heart beat was normal. Routine laboratory examinations, including HIV serology tests, found no abnormalities. Swabs from the ulcer were positive for acid-fast bacilli by Ziehl–Neelsen stain, and for *IS 2404* (DNA sequence specific for *Mycobacterium ulcerans*) by polymerase chain reaction testing, but no growth of *M. ulcerans* was obtained on culture. Histopathological analysis of punch biopsy specimens showed typical features of Buruli ulcer.

As streptomycin is contraindicated in pregnancy, we treated the patient with a combination of oral rifampicin (600 mg daily) and oral clarithromycin (500 mg twice daily) for 56 days, beginning 2 weeks after presentation. The treatment was well tolerated. We monitored the clinical response through serial photographs (Box 1) and measurements of the circumference of the affected and unaffected limbs at defined points (Box 2).

The patient gave birth to a healthy boy weighing 2.25 kg in September 2007, 2 weeks after completing antibiotic treatment. She underwent skin grafting a month later. The lesion healed without functional limitation (Box 1, D), and the patient was discharged in December 2007. At that time, the surface area affected by the lesion was reduced by 55%.

To our knowledge, this is the first report of successful treatment of Buruli ulcer using fully oral treament with rifampicin and clarithromycin alone. We hope our experience will contribute to future discussion and studies to find an oral treatment for this devastating disease.

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Ange D Dossou, Medical Officer[1]
Ghislain E Sopoh, Medical Officer[1]
Christian R Johnson, Medical Officer[2]
Yves T Barogui, Medical Officer[3]
Dissou Affolabi, Assistant Professor of Biology[4]
Sévérin Y Anagonou, Professor of Bacteriology–Virology[4]
Théophile Zohoun, Professor of Public Health[5]
Françoise Portaels, Professor of Microbiology[6]
Kingsley Asiedu, Medical Officer[7]

1 Centre de Dépistage et de Traitemente de l'Ulcère, Allada, Benin.
2 Programme National de Lutte contre la Lépre et l'Ulcère de Buruli, Cotonou, Benin.
3 Centre de Dépistage et de Traitemente de l'Ulcère, Lalo, Benin.
4 Laboratoire de Référence des Mycobactéries, Cotonou, Benin.
5 Faculté des Sciences de la Santé, Cotonou, Benin.
6 Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium.
7 Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland.
cdtuballada@yahoo.fr

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