

The Emerging Threat of Untreatable Gonococcal Infection

TO THE EDITOR: In their summary of the global threat of antibiotic-resistant *Neisseria gonorrhoeae*, Bolan et al. (Feb. 9 issue)¹ state that “in patients who are allergic to cephalosporins, the only option is 2 g of azithromycin orally.” However, the aminoglycoside spectinomycin (unavailable in the United States since 2006) has proven efficacy against genital gonococcal infection² and is recommended for patients in the United Kingdom who are allergic to penicillin.³ Since most gonococcal isolates remain susceptible to spectinomycin, it represents a viable option for cephalosporin-resistant genital gonorrhea,^{2,3} although ongoing uncertainty regarding manufacturing and supply may compromise its future usefulness.⁴ In addition, reduced efficacy against pharyngeal infection has been observed.² On a practical level, determining each isolate’s specific antimicrobial sensitivity profile in the context of penicillin al-

lergy or third-generation cephalosporin resistance is advisable, since cephalosporin-resistant isolates may retain susceptibility to other common agents.³

Sarah Duncan, M.B., Ch.B.

Churchill Hospital
Oxford, United Kingdom

Christopher J. Duncan, M.B., Ch.B.

University of Oxford
Oxford, United Kingdom
chrisduncan@doctors.net.uk

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Lower-Extremity Lymphedema and Elevated Body-Mass Index

TO THE EDITOR: Lymphedema is a disease caused by the anomalous development of the lymphatic system or injury to the lymphatic vasculature; millions of people are affected worldwide.¹ In this condition, fluid accumulates in the interstitial space, causing enlargement of the affected area. Complications include functional disability, psychosocial disorders, infection, skin changes, and, rarely, malignant transformation. Primary (idiopathic) lymphedema is rare, with an incidence of 1.2 cases per 100,000 persons younger than 20 years of age.² Secondary lymphedema is more common and results from injury (e.g., infection or radiation) or the removal of lymph nodes or lymphatic vasculature.

We report on 15 obese patients (body-mass index [BMI; the weight in kilograms divided by the square of the height in meters], >30)³ with bilateral lower-extremity enlargement who were referred to our center. Twelve of the 15 were women, and the mean age was 57.9 years (range, 34 to 78); the mean BMI was 51.4 (range, 30.7 to 88.1). None of the patients had a history of primary lymphedema, inguinal lymphadenectomy or radiation, or ulceration of a lower extremity. All patients underwent lymphoscintigraphy, which

has been reported to be 100% specific and 92% sensitive for lymphedema.^{4,5}

Five patients had abnormal results on lymphoscintigraphy that showed impaired lymphatic function consistent with lymphedema; 10 had normal results (Table 1; and see the figure in the Supplementary Appendix, available with the full text of this letter at NEJM.org). The average BMI of the patients with lymphedema (70.1 [range, 59.7 to 88.1]) was significantly greater than the BMI of obese patients without lymphedema (42.0 [range, 30.7 to 53.3]) ($P < 0.001$). All patients with a BMI above 59 had lymphedema, whereas each patient with a BMI less than 54 had normal lymphatic function. There was no difference between the groups with respect to sex ($P = 1.00$) or age ($P = 0.29$).

Our findings suggest that obesity, which affects one third of the population in the United States,³ may be a cause of lower-extremity lymphedema. As BMI increases, there might be a threshold above which lymphatic flow becomes impaired. Proximal transport of lymphatic fluid from the extremity is dependent on the function of the lymphatic vasculature (clearance) and the volume of lymph produced by the tissues (load).

Table 1. Patients' Age, BMI, and Lymphoscintigraphic Results.*

Patient No.	Age yr	BMI	Lymphoscintigraphic Result
1	63	30.7	Negative
2	53	33.5	Negative
3	56	33.8	Negative
4	34	35.2	Negative
5	61	36.1	Negative
6	56	48.4	Negative
7	55	48.5	Negative
8	44	50.1	Negative
9	78	50.2	Negative
10	56	53.3	Negative
11	44	59.7	Positive
12	71	61.0	Positive
13	64	63.4	Positive
14	64	78.3	Positive
15	69	88.1	Positive

* The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. The mean age of patients with negative results on lymphoscintigraphy was 55.6 years (range, 34 to 78), and the mean BMI was 42.0 (range, 30.7 to 53.3). The mean age of patients with positive results on lymphoscintigraphy was 62.4 years (range, 44 to 71), and the mean BMI was 70.1 (range, 59.7 to 88.1).

As the amount of adipose tissue increases in the lower extremity, lymphatic vessels may become dysfunctional (possibly because of compression or inflammation), thereby reducing proximal lymphatic flow. Alternatively, elevated production of lymph from an enlarging limb may overwhelm the capacity of a normal lymphatic system to remove the fluid from the extremity. Although lymphedema is typically progressive, we speculate that major weight loss (e.g., after a bariatric procedure) might reverse lymphatic insufficiency in obese patients with this condition.

Arin K. Greene, M.D.
Frederick D. Grant, M.D.
Sumner A. Slavin, M.D.

Children's Hospital Boston
Boston, MA
arin.greene@childrens.harvard.edu

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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CORRECTIONS

Prostate-Cancer Mortality at 11 Years of Follow-up (March 15, 2012;366:981-90). In Figure 2 (page 988), the range of values given on the y axis for the Cumulative Hazard of Death from Prostate Cancer should have been from 0.000 to 0.014, rather than from 0.00 to 0.14. We regret the error. The article is correct at NEJM.org.