Original Investigation

Insulin Resistance and Metabolic Syndrome in Young Men With Acne

Mohit Nagpal, MD; Dipankar De, MD; Sanjeev Handa, MD; Arnab Pal, MD, PhD; Naresh Sachdeva, PhD

INTRODUCTION Robust evidence of the association of insulin resistance and metabolic syndrome with acne in male patients is lacking.

OBJECTIVE To assess the prevalence of metabolic syndrome and insulin resistance in male patients 20 years or older with acne.

DESIGN, SETTING, AND PARTICIPANTS We performed a cross-sectional study in 100 male patients with acne and 100 age-matched male controls without acne from a dermatology outpatient department of a tertiary care institute. Postadolescent patients were recruited only to negate the effects of physiologic insulin resistance that are seen at the time of puberty and adolescence. Twenty-five patients were included in each of the 4 individual severity groups according to the Global Acne Grading System and were age matched to 100 male controls without acne.

EXPOSURES Clinical examination, Global Acne Rating System, National Cholesterol Education Programme Adult Treatment Panel III (NCEP-ATP III), and Homeostasis Model Assessment–Insulin Resistance (HOMA-IR).

MAIN OUTCOMES AND MEASURES Metabolic syndrome was diagnosed as per the criteria of the modified NCEP-ATP III. Insulin resistance was assessed by the HOMA-IR. A HOMA-IR value greater than 2.5 was arbitrarily considered as insulin resistance.

RESULTS Prevalence of insulin resistance was significantly higher in cases (22%) compared with controls (11%) (P = .03). The prevalence of metabolic syndrome was comparable between cases (17%) and controls (9%) (P = .09). Prevalence of insulin resistance and metabolic syndrome did not differ significantly among the acne severity groups.

CONCLUSIONS AND RELEVANCE Postadolescent male patients with acne more commonly have insulin resistance. This resistance may be a stage of prediabetes, and the patients may develop hyperinsulinemia or type 2 diabetes in the future. These patients should be followed up for a prolonged time to determine whether they develop conditions associated with insulin resistance.

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Author Affiliations: Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh, India (Nagpal, De, Handa); Department of Biochemistry, Postgraduate Institute of Medical Education and Research, Chandigarh, India (Pal); Department of Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh, India (Sachdeva).

Corresponding Author: Dipankar De, MD, Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh, India, PIN-160012 (dr_dipankar_de@yahoo.in).

JAMA Dermatol. 2016;152(4):399-404. doi:10.1001/jamadermatol.2015.4499
Published online December 23, 2015.

Acne, a disorder of pilosebaceous units, is one of the common skin disorders worldwide and is seen primarily in adolescents. Androgens have been recognized to increase the size of sebaceous glands, increase sebum production, and stimulate keratinocyte proliferation, thereby causing acne. Physiologic insulin resistance during puberty leads to hyperinsulinemia, which in turn leads to increased androgen synthesis[1]; both hyperinsulinemia and hyperandrogenemia lead to acne formation. Hyperinsulinemia increases the level of free insulin-like growth factor 1 (IGF-1) and decreases the level of insulin-like growth factor binding protein 3.[2] Insulin-like growth factor 1 increases the mean facial sebum excretion rate, increases serum levels of dihydrotestosterone and dehydroepiandrosterone sulfate, and causes sebocyte proliferation.[3] Hyperinsulinemia also increases levels of epidermal growth factors and transforming growth factor β, which elevate levels of plasma nonesterified fatty acids, thus causing inflammation and acne.[4] Insulin resistance plays a pivotal role in the cluster of metabolic abnormalities that are components of the metabolic syndrome.

Metabolic syndrome forms an integral part of polycystic ovarian syndrome. Impaired hypothalamic-pituitary-adrenal axis and ovarian steroidogenesis along with insulin resistance are implicated in the pathogenesis of polycystic ovarian syndrome.[5] Polycystic ovarian syndrome is a common entity in women, and acne is commonly seen in this syndrome.[6] In males, the association between insulin resistance and acne has been poorly investigated. A study[7] with limited sample size and without age consideration of patients found that most patients with acne had decreased insulin sensitivity and impaired metabolic profile in the form of higher body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]), waist circumference, waist-hip ratio, systolic blood pressure, diastolic blood pressure, basal and 120-minute oral glucose tolerance test results, serum insulin concentrations, basal glucose concentrations, and Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) values and lower high-density lipoprotein cholesterol (HDL-C) levels.

The present larger study was undertaken to investigate the prevalence of insulin resistance and metabolic syndrome in postadolescent male patients with acne and to assess the differential prevalence of insulin resistance and metabolic syndrome in different severities of acne. Because insulin resistance occurs physiologically during puberty and assessment of prevalence of insulin resistance was one of the objectives of our study, we only included postadolescent patients (ie, aged ≥20 years) to annul the effects of peripuberty physiologic insulin resistance.

Methods

After approval was obtained from the Postgraduate Institute of Medical Education and Research Institutional Ethics Committee (Intramural), 100 male patients with acne and 100 aged-matched male controls without acne were recruited from the patients attending the Dermatology Outpatient Department of the Department of Dermatology, Postgraduate Institute of Medical Education and Research. The diagnosis of acne was purely based on clinical examination by experienced dermatologists (D.D., S.H.). Controls were patients attending the Dermatology Outpatient Department for nonacne dermatoses who had not previously had acne. All the study participants (cases and controls) with a history of smoking, liver disorders, malignant neoplasms, thyroid disorders, Cushing syndrome, and acromegaly and who had received treatment with isotretinoin therapy in the preceding year were excluded from the study because these conditions lead to the alteration in levels of insulin and/or IGF-1 and hence may affect insulin resistance status. Written informed consent was obtained from all the participants in the study. All patients were subjected to detailed history taking and clinical examination. Clinical examination included measurement of height, weight, waist circumference and blood pressure as well as determination of clinical severity of acne by the Global Acne Grading System.[8] Patients were recruited consecutively until 25 patients were included in each of the 4 individual acne severity groups: mild, moderate, severe, and very severe. Total number of cases included was therefore 100.

According to Indian guidelines, a BMI of 23 through 24.9 is overweight, a BMI of 25 through 29.9 is moderate obesity, and a BMI of 30 or higher is severe obesity.[9] The waist circumference was measured by placing the measuring tape snugly around the abdomen at the level of the iliac crest. The blood pressure was taken with the patient in the sitting posture by a mercury sphygmomanometer.

Metabolic syndrome was diagnosed as per the criteria of the modified National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III)[10] and requires at least 3 of the following: central obesity (waist circumference of ≥102 cm [male] [modified for Asians: men >90 cm])[9]; dyslipidemia (triglyceride levels ≥150 mg/dL [to convert to millimoles per liter, multiply by 1.8) or drug treatment for elevated levels; dyslipidemia (HDL-C levels <40 mg/dL [to convert to millimoles per liter, 0.0259] [male]) or drug treatment for elevated levels; blood pressure of 130/85 mm Hg or higher or drug treatment for hypertension; fasting plasma glucose level of 100 mg/dL or higher (to convert to millimoles per liter, multiply by 0.0555); and/or drug treatment for diabetes mellitus.

Estimation of biochemical parameters (fasting serum triglycerides, HDL-C, and plasma glucose levels) was performed using an Olympus AU2700 Plus analyzer (Beckman Coulter Inc), which is certified by the International Organization for Standardization, after proper quality control and calibration as per standard operating protocol. Insulin levels were estimated with an electrochemiluminescence immune assay.

The HOMA-IR values were calculated using the following formula: Fasting Insulin (Microunits per Milliliter) × Fasting Glucose (Micograms per Deciliter)/405. A HOMA-IR value greater than 2.5 was predefined arbitrarily as insulin resistance.

Table 1. Study Parameters in Cases and Controls[a]

Parameters	Cases	Controls	*P* Value
Age, y	22.7 (3.0) [22.1-23.3]	23.7 (3.0) [23.1-24.3]	.06
Height, m	1.7 (0.1) [1.69-1.71]	1.7 (0.1) [1.67-1.70]	.16
Weight, kg	66.7 (13.1) [64.1-69.3]	67.0 (10.9) [64.8-69.2]	.85
BMI	22.9 (4.0) [22.1-23.7]	23.4 (3.2) [22.7-24.0]	.37
Waist circumference, cm	85.3 (9.4) [83.4-87.2]	83.6 (7.4) [82.2-85.1]	.17
SBP, mm Hg	120.2 (10.3) [118.2-122.2]	116.9 (9.1) [115.1-118.7]	.01
DBP, mm Hg	79.1 (7.0) [77.7-80.5]	76.2 (5.9) [75.1-77.4]	.002
Serum triglycerides, mg/dL	106.0 (54.2) [95.2-116.7]	120.8 (53.6) [110.1-131.4]	.05
Serum HDL-C, mg/dL	42.5 (11.3) [40.2-44.7]	40.8 (8.6) [39.1-42.5]	.24
Fasting plasma glucose, mg/dL	88.2 (8.3) [86.6-89.9]	84.5 (11.2) [82.3-86.7]	.008
Fasting plasma insulin, μIU/mL	9.2 (8.5) [7.5-10.8]	7.8 (6.8) [6.5-9.2]	.22
HOMA-IR	2.0 (1.8) [1.6-2.3]	1.7 (2.3) [1.3-2.2]	.049
Insulin resistance (predefined as HOMA-IR values >2.5), %	22	11	.04
Metabolic syndrome assessed by NCEP-ATP III, %	17	9	.09

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, Homeostasis Model Assessment–Insulin Resistance; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; SBP, systolic blood pressure.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; HDL-C to millimoles per liter, multiply by 0.0259; plasma insulin to picomoles per liter, multiply by 6.945; and triglycerides to millimoles per liter, multiply by 0.0113.

[a] Data are presented as mean (SD) [95% CI] unless otherwise indicated.

The normality of the measurable data was assessed with the Kolmogorov-Smirnov test. Because measurable parameters were normally distributed, group means were compared by the *t* test (unpaired). The comparison of various categorical and classified data between the case and control groups was analyzed with the χ^2 test. The comparison of parameters, such as weight and height among the acne severity groups, was analyzed with analysis of variance. $P < .05$ was considered as significant in all tests.

Results

A total of 100 male patients with acne (aged 20-32 years) and 100 age-matched controls without acne were included in the study. There was no significant statistical difference in age, height, and weight between cases and controls (**Table 1**). The mean (SD) BMI in cases (22.9 [4.0]) was comparable to controls (23.4 [3.2]) ($P = .37$) (Table 1). Mean (SD) systolic blood pressure (SBP) and diastolic blood pressure (DBP) of cases were 120.2 (10.3) mm Hg and 79.1 (7.0) mm Hg, respectively, and were statistically significantly higher than those of controls (ie, 116.9 [9.1] mm Hg and 76.2 [5.9] mm Hg, respectively) ($P = .01$ and .002, *t* test, respectively; Table 1). Mean (SD) fasting plasma glucose levels were significantly higher in patients (88.2 [8.3] mg/dL) than in controls (84.5 [11.2] mg/dL) ($P = .008$; Table 1). However, mean (SD) fasting insulin levels were comparable between the cases (9.2 [8.5] μIU/mL; to convert to picomoles per liter, multiply by 6.945) and controls (7.8 [6.8] μIU/mL) ($P = .22$; Table 1). Of interest, the mean (SD) HOMA-IR value in cases was significantly higher (2.0 [1.8]) than in controls (1.7 [2.3]) ($P = .049$; Table 1). Insulin resistance, which was arbitrarily predefined for our study as a HOMA-IR value greater than 2.5, was seen in 22% cases and 11% controls, and this difference in prevalence was statistically significant ($P = .036$; Table 1). The prevalence of metabolic syndrome was 17% in cases and 9% in controls, a difference that was not statistically significant ($P = .09$; Table 1). It was observed that there was no significant difference in mean age of patients in the 4 groups of acne. Mean weight was observed to be significantly different among the different severity groups ($P = .04$; **Table 2**). On post hoc testing, it was observed that the mean weights in mild and very severe acne groups were significantly different, with mean weight being higher in the very severe acne group compared with that in the mild acne group ($P = .02$). The mean BMI in the very severe acne group was significantly higher than that in mild acne group ($P = .04$). The mean height, waist circumference, SBP, and DBP did not differ significantly among the different acne severity groups ($P = .67$, .17, .20, and .20, respectively; Table 2). The mean fasting plasma glucose level in all individual acne severity groups was higher than the mean fasting plasma glucose level in controls. Prevalence of insulin resistance ($P = .55$) and metabolic syndrome ($P = .38$) did not differ among the acne severity groups (Table 2).

Discussion

Our cross-sectional study to identify the prevalence of insulin resistance and metabolic syndrome in male patients 20 years or older with acne was prompted by the common finding of acne in women with polycystic ovarian syndrome, an endocrinologic abnormality in which insulin resistance may be causal for development of acne.[11] Although mean weight and BMI were comparable between cases and controls, these parameters were significantly higher in cases with

Table 2. Study Parameters in 4 Acne Severity Group[a]

Parameter	Mild	Moderate	Severe	Very Severe	*P* Value
Age, y	23.0 (3.4) [21.6-24.4]	22.2 (3.1) [20.9-23.5]	23.0 (2.5) [22.0-24.0]	22.6 (3.2) [20.3-23.9]	.73
Height, m	1.7 (0.1) [1.66-1.72]	1.7 (0.1) [1.66-1.73]	1.7 (0.1) [1.67-1.74]	1.7 (0.1) [1.68-1.74]	.68
Weight, kg	61.8 (9.8) [57.8-65.9]	66.6 (10.3) [62.3-70.9]	66.1 (14.3) [60.2-72.0]	72.2 (15.7) [65.7-78.7]	.04
BMI	21.5 (2.7) [20.4-22.6]	23.2 (3.9) [21.6-24.8]	22.4 (3.9) [20.8-24.1]	24.4 (4.8) [22.5-26.4]	.06
Waist circumference, cm	82.2 (6.4) [79.6-84.9]	87 (7.7) [83.8-90.2]	84.5 (10.8) [80.0-89.0]	87.5 (11.2) [82.9-92.1]	.17
SBP, mm Hg	117.9 (7.6) [114.8-121.1]	120.9 (8.1) [117.5-124.2]	123.5 (11.9) [118.6-128.5]	118.5 (12.3) [113.4-123.6]	.20
DBP, mm Hg	76.7 (6.8) [73.9-79.5]	80.8 (5.0) [78.8-82.9]	79.8 (6.5) [77.1-82.5]	79.0 (9.1) [75.2-82.7]	.20
Fasting plasma glucose, mg/dL	88.2 (6.8) [85.4-91.0]	87.4 (9.1) [83.7-91.2]	90.9 (9.0) [87.2-94.6]	86.4 (7.9) [83.1-89.6]	.25
Serum HDL-C, mg/dL	40.6 (8.4) [37.1-44.0]	44.2 (13.1) [38.8-49.6]	42.0 (9.1) [38.3-45.8]	43.2 (14.0) [37.4-49.0]	.69
Serum triglycerides, mg/dL	114.9 (64.6) [88.3-141.6]	104.1 (43.8) [86.1-122.2]	100.6 (59.0) [76.3-125.0]	104.2 (49.1) [84.0-124.5]	.81
Plasma insulin, μIU/mL	7.0 (3.9) [5.4-8.6]	9.0 (5.2) [6.9-11.1]	9.3 (6.4) [6.6-12.0]	11.4 (14.3) [5.5-17.3]	.34
HOMA-IR	1.5 (0.8) [1.2-1.9]	1.9 (1.2) [1.4-2.4]	2.1 (1.4) [1.5-2.6]	2.4 (2.9) [1.2-3.6]	.39
Insulin resistance (predefined as HOMA-IR values ≥2.5), %	18.2	22.7	36.4	22.7	.55
Metabolic syndrome assessed by NCEP-ATP III, %	17.6	17.6	23.5	41.2	.38

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, Homeostasis Model Assessment–Insulin Resistance; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; SBP, systolic blood pressure.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; HDL-C to millimoles per liter, multiply by 0.0259; plasma insulin to picomoles per liter, multiply by 6.945; and triglycerides to millimoles per liter, multiply by 0.0113.

[a] Data are presented as mean (SD) [95% CI] unless otherwise indicated.

Table 3. Findings of the Present Study Compared With Those by Del Prete et al[7] and Balta et al[12]

	Present Study, Mean (SD)			Previous Study by Del Prete et al, Mean (SD)			Previous Study by Balta et al, Mean (SD)		
Parameter	Cases	Controls	*P* Value	Cases	Controls	*P* Value	Cases	Controls	*P* Value
No. of study subjects	100	100		22	22		35	35	
Age, y	22.7 (3.0)	23.7 (3.0)	.06	18.6 (2.5)	20.2 (3)	.06	30.8 (5.4)	30.8 (5.8)	.98
BMI	22.9 (4.0)	23.4 (3.2)	.37	24 (2.8)	20.1 (1.5)	.003	24.6 (4.0)	25.0 (4.1)	.68
Waist circumference, cm	85.3 (9.4)	83.6 (7.4)	.17	86.8 (9.8)	83.4 (8)	.002	…	…	…
SBP, mm Hg	120.2 (10.3)	116.9 (9.1)	.01[a]	128.1 (7.9)	112.5 (9)	.0001	…	…	…
DBP, mm Hg	79.1 (7.0)	76.2 (5.9)	.002[a]	80.9 (6.4)	72.9 (7.8)	.001	…	…	…
Fasting plasma glucose, mg/dL	88.2 (8.3)	84.5 (11.2)	.008[a]	88.9 (7.8)	84.3 (5.9)	.03	89.7 (7.4)	90.0 (12.6)	.90
HDL-C, mg/dL	42.5 (11.3)	40.8 (8.6)	.24	46.5 (8)	57.3 (8)	.001	53.4 (19.6)	53.0 (12.2)	.91
Triglycerides, mg/dL	106.0 (54.2)	120.8 (53.6)	.05	83 (3.2)	78.5 (22.3)	.40	123.7 (94.6)	94.0 (59.5)	.12
Plasma insulin, μIU/mL	9.2 (8.5)	7.8 (6.8)	.22	10.6 (8.4)	5.5 (1.4)	.01	9.0 (4.9)	9.8 (3.5)	.41
HOMA-IR	2.0 (1.8)	1.7 (2.3)	.04[a]	1.7 (0.8)	1.1 (0.3)	.01	2.0 (1.2)	2.1 (0.8)	.51
Metabolic syndrome, %	17	9	.09	36	0	…	…	…	…

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high--density lipoprotein cholesterol; HOMA-IR, Homeostasis Model Assessment–Insulin Resistance; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; SBP, systolic blood pressure. Ellipses indicate not applicable.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; HDL-C to millimoles per liter, multiply by 0.0259; insulin to picomoles per liter, multiply by 6.945; and triglycerides to millimoles per liter, multiply by 0.0113.

[a] Similar results in terms of statistical significance between our study and that by Del Prete et al.[7]

very severe acne compared with those with mild acne. Another important observation was significantly higher SBP and DBP in cases. The mean fasting plasma glucose level was significantly higher in cases. Although the mean fasting plasma insulin level was higher in cases, it was not statistically significant. Because HOMA-IR depends on the product of these 2 parameters (ie, fasting plasma glucose and insulin levels), expectedly the mean HOMA-IR value was significantly higher in cases. However, the HOMA-IR value was comparable among acne severity groups. Significantly higher prevalence of insulin resistance, which was predefined as a HOMA-IR value greater than 2.5, was observed in cases. However, overrepresentation of insulin resistance in more severe acne compared with milder acne was not observed. Although the proportion of participants with metabolic syndrome according to modified NCEP-ATP III

criteria was higher in cases than in controls, the difference was not statistically significant.

The salient observations of our study have been compared with those of Del Prete et al[7] and Balta et al[12] (**Table 3**). In the study by Del Prete et al,[7] 22 male patients were recruited within the age group of 15 to 26 years, with a mean age of 18.6 years. To determine insulin resistance in acne, Balta et al[12] recruited 35 male and female patients with acne 25 years or older. The mean age of the patients was 30.8 years. Balta et al[12] did not observe a statistical difference between cases and controls in mean of any of the study parameters (ie, BMI, HDL-C, triglycerides, fasting plasma glucose, and insulin levels, and HOMA-IR). Observation of statistically significant difference between cases and controls in the parameters SBP, DBP, fasting plasma glucose, and HOMA-IR by Del Prete et al[7] was similar to our findings. In addition, they observed significantly higher BMI, waist circumference, HDL-C level, and plasma insulin level in cases. Higher BMI in acne cases has also been observed by Tsai et al.[13] Alan et al[14] observed a positive correlation between BMI and severity of acne. However, Balta et al[12] did not find any association between BMI and severity of acne. In our study, acne cases had a higher proportion of metabolic syndrome according to modified NCEP-ATP III criteria, although the difference of proportion was not statistically significant. Prevalence of metabolic syndrome was comparable among acne severity groups. To our knowledge, no earlier study has evaluated the differential prevalence of metabolic syndrome based on severity of acne.

The prevalence of metabolic syndrome is strictly age dependent and increases sharply after 60 years of age.[15] An Indian study[16] performed in a general urban population in eastern India found a prevalence rate of 6.7% in the age group of 20 through 29 years, peaking at 65.6% in the age group of 60 through 69 years. In our study, the prevalence of metabolic syndrome in patients with acne (17%) was more than 2 times the prevalence in the same age group (6.7%) as observed in the above mentioned study. The prevalence of metabolic syndrome in patients with acne reported by Del Prete et al[7] was much higher at 36%. The reason for the significantly high prevalence of metabolic syndrome in their study may be the fact that a diagnosis of metabolic syndrome was made even when 2 of 5 features were present in place of the recommended 3. Another drawback of their study is the sample size, which is considered too low for a study assessing prevalence. In insulin resistance, there is increased release of insulin owing to decreased sensitivity. This can further lead to increased production of IGF-1.[2] Increased levels of both insulin and IGF-1 lead to acne in an interconnected regulated fashion.[17]

A limitation of this study is the cross-sectional study design. Future studies will follow up patients with acne to assess the development of clinical conditions associated with insulin resistance (eg, acanthosis nigricans) and metabolic syndrome.

Conclusions

Postadolescent male patients with acne are more prone to have higher mean HOMA-IR values, higher mean fasting plasma glucose levels, higher prevalence of insulin resistance, and higher mean SBP and DBP compared with controls. Body weight tends to be higher in those with more severe grades of acne. Prevalence of insulin resistance and metabolic syndrome does not significantly vary with acne severity. Insulin resistance may be a stage of prediabetes, and the patients may develop hyperinsulinemia or type 2 diabetes in the future. These patients should be followed up to determine whether they develop conditions associated with insulin resistance.

ARTICLE INFORMATION

Accepted for Publication: September 23, 2015.

Published Online: December 23, 2015. doi:10.1001/jamadermatol.2015.4499.

Author Contributions: Drs Nagpal and De had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Nagpal, De, Handa.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Nagpal.
Critical revision of the manuscript for important intellectual content: De, Handa, Pal, Sachdeva.
Statistical analysis: Nagpal, De.
Administrative, technical, or material support: De, Handa, Pal.
Study supervision: De, Handa, Pal, Sachdeva.

Conflict of Interest Disclosures: None reported.

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NOTABLE NOTES

Syphilis, a Disfiguring Disease

Chu Hsiao, BS; Samantha Hsieh, BS; Eric L. Maranda, BS; Victoria Lim, BS; Joseph Zullo, BS; Joaquin Jimenez, MD

After reeling from the Black Plague in the early 15th century, the medical community was faced with another epidemic. This one likely traveled with Christopher Columbus and his crew across the seas from the Americas to Europe. There was no consensus for the name of the disease. Countries each referred to the disease as originating from a neighboring country, reflecting the political rivalries at the time. For example, the French disease, the Neapolitan disease, the Polish disease, the German disease, and the Spanish disease all referred to the same unfamiliar malady.[1,2] The disease adopted its more infamous name in 1530 from Girolamo Fracastoro's poem in which the god Apollo curses the people with a monstrous ailment called syphilis to punish a shepherd named Syphilis for worshipping a king.[2]

Syphilis was met with fear and stigmatizing disgust as it spread quickly and with a fatality much greater than the syphilis of today. The illness disfigured bodies with eruptions of pustules, ulcerated chancres and facial destruction. Syphilis was so terrifying that even physicians initially refused to treat patients with this disease. Governing authorities were as concerned about containing infection as they were about keeping the afflicted out of sight.[3] By the late 18th century, syphilis' symptoms, ability to infect internal organs, and congenital and nonsexual modes of transmission were well documented and distinguished from other venereal causes. However, it was not until 1905 that the etiologic origin was identified as *Spirochaeta pallida*.[1]

While the rich could hide in their homes and receive treatment from the best physicians, the poor were left searching for a cure from anyone else—midwives, spice merchants, unlicensed practitioners, apothecaries, or barber-surgeons. Viewed largely as a cutaneous affliction, many of the earlier cases were treated by barber-surgeons. Popular treatments utilized mercury and guaiac "holy" wood. Mercury was thought to remedy skin disorders and was often administered topically, though it was given via fumigation in some instances. Guaiac wood imported from the Indies was thought to cure syphilis by purging the body.[3] When fever was noted to improve the symptoms of later disease stages, such as neurosyphilis, treatments began to include various pyrogenic methods. One notable procedure developed in the early 1900s required infecting syphilitic patients with malaria to induce fever paroxysms and subsequently treating the malaria with quinine. However, no treatment was as effective as the introduction of penicillin in the mid-1900s by Alexander Fleming.[2]

Despite being a tremendously horrifying and novel disease when it first appeared in Europe, syphilis was greeted by a force of physicians who rationalized the disease using the existing tools and explanatory framework of their time. Their findings paved the way for the discovery of penicillin, which is still widely used to treat syphilis today.

Author Affiliations: Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida.

Corresponding Author: Eric L. Maranda, BS, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, 1475 NW 12th Ave, Miami, FL 33136 (emaranda@med.miami.edu).

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