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The Gravity of Weight

Fat: Death in the Time of COVID-19

Those with excessive weight are more vulnerable.

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Nineteenth century Belgian artist Antoine Wiertz, "The Premature Burial," 1854. The person depicted was suffering from cholera. Wiertz Museum, Brussels, part of the Royal Museums of Fine Arts, Belgium.
Source: Wikimedia Commons

"... there are so many we shall have to mourn, when grief has been made so public ... of whom shall we speak?" (W.H. Auden, from his collection, *Another Time,* 1940)

When British-American poet W.H. Auden wrote his elegy, *In Memory of Sigmund Freud*, he had in mind not only the singular death of Freud, who fled Nazi-occupied Vienna and died in exile in London in 1939, but the mounting death toll and the devastating effects of war and injustice as Hitler savaged Europe.

Though we are not at war, it may seem so as COVID-19 continues to claim its victims, and as I write this, protestors throughout the world march to decry the brutality of unbridled racism. “For every day they die among us ...” wrote Auden. Public health officials warn that these mass gatherings, without proper social distancing, will inevitably lead to the further spread of COVID-19.

For complex social, economic, and medical reasons, some of which we still do not understand, COVID-19 preferentially affects minorities, the elderly, and those with pre-existing chronic conditions, such as those whose immune systems are compromised or those who have cancer, diabetes, asthma, heart disease, kidney damage, or hypertension. (Malavazos et al, *Obesity*, 2020) Undoubtedly, genetic factors are involved. For example, there is even a recent report that certain blood groups (e.g., type O) may be more protective and others (e.g., type A) may present more risk for respiratory failure with COVID-19. (Ellinghaus et al, *medRxiv*, preprint, 2020) What clinicians, though, have also noticed is that those who are overweight—and particularly those who are obese—are more vulnerable to the destructive effects of this virus. (Malavazos et al, 2020) While diseases such as type

2 diabetes and hypertension, for example, often co-occur with obesity and confound or "at least make more difficult identification of the independent role of obesity," obesity itself seems to lead to a worse outcome. (Malavazos et al, 2020) "The role of obesity in COVID-19 must not be ignored." (Kassir, *Obesity Reviews*, 2020)

Color etching of Daniel Lambert at age 36. Lambert weighed 739 pounds at the time of his death, at age 39. He was considered "the most corpulent man of whom an authentic record exists," according to the "Dictionary of National Biography." Those who are severely obese are much more vulnerable to COVID-19 and more likely to require mechanical ventilation and to die from the disease.
Source: Wellcome Trust Collection/Creative Commons

Remarkably, and despite heroic efforts, "not a single nation" has managed to reduce the prevalence of obesity in the past 20 years. (Aleksandrova et al, *Clinical Chemistry*, 2018) This has translated into 1.9 billion people worldwide who are either overweight or obese, including more than 50 million children under the age of 5. (Saltiel and Olefsky, *The Journal of Clinical Investigation,* 2017) Heymsfield and colleagues (D. Ryan et al, *Obesity,* 2020) report that in 2017-18, the obesity prevalence in the U.S. alone was 42.4%. For some researchers, such as David L. Katz, M.D., MPH, we are in the midst of two pandemics—"the global burden of chronic disease," such as obesity, and COVID-19.

Initially, clinicians from China did not specifically single out obesity in case reports of COVID-19; they had not provided data on height and weight so that body mass index (BMI), a proxy measure for the amount of fat in the body, could be calculated. (Stefan et al, *Nature Reviews/Endocrinology,* 2020) By convention, obesity is defined as a BMI of 30 kg/m^2 or greater, with higher levels divided into Class I, II, and III. Obesity levels for Asians are set at a lower level. (Zheng et al, *Metabolism Clinical and Experimental*, 2020)

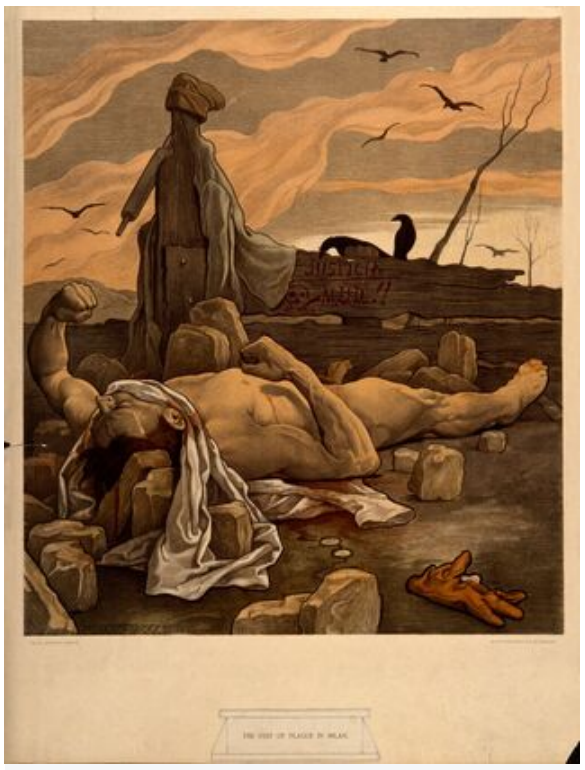
Epidemiological data from the U.S., though, now implicate obesity in at least 25% of patients who die from COVID-19. (P. Ryan and Caplice, *Obesity*, 2020) Further, clinicians with data from 265 patients among several university hospitals around the U.S., including Johns Hopkins, University of Pennsylvania, and New York University, found that younger patients who were admitted to the hospital with COVID-19 were more likely to be obese; obesity is an “under-appreciated risk factor for COVID-19.” (Kass et al, *The Lancet,* 2020) Likewise, in another N.Y. population of 572 patients younger than 50 years, a BMI above 40 kg/m^2 (Class III) was independently associated with mortality. (Klang et al, *Obesity*, 2020)

British artist James Gillray, "A Sphere, Projecting Against a Plane," January 3, 1792.
Source: Metropolitan Museum of Art, NYC/Public Domain. Credit line: Gift of Philip van Ingen, 1942.

A retrospective study of 770 patients with COVID-19 from Weill Cornell (NY) found obese patients were more apt to be symptomatic with fever, cough, and shortness of breath and had significantly higher rates of ICU admission and need for mechanical ventilation, even after adjusting for age and race, among other confounding variables. Obesity was an independent predictor of ICU admission, ventilation, and death. (Hajifathalian et al, *Obesity,* 2020)

Data from other countries, such as France, confirm that disease severity is associated with increased BMI, particularly when BMI is greater or equal to 35 kg/m^2 (Class II obesity): in a retrospective study of 124 patients, obesity was “unexpectedly frequent” in patients admitted to intensive care; the need for "invasive mechanical ventilation" was associated with obesity, independent of age, sex, diabetes, and hypertension. (Simonnet et al, *Obesity*, 2020)

Researchers have known for years that obesity, as a state of chronic, low-grade systemic inflammation, (O'Rourke, *Surgery*, 2009) was an independent risk factor for hospitalization and even death in earlier influenza pandemics, such as with H1N1 in 2009. (Kassir, 2020; Hajifathalian et al, 2020; Huttunen and Syrjänen, *International Journal of Obesity*, 2013). This was seen in a California sample of 534 adults where, even after adjusting for co-morbidity, extreme obesity with a BMI of 40 kg/m^2 or more (Class III) was independently and significantly associated with death. (Louie et al, *Clinical Infectious Diseases*, 2011)



Dying man stoned on suspicion of spreading the plague. Colour lithograph after F. Jenewein, 1899.
Source: Wellcome Trust Collection/Public Domain

In general, obese patients may be harder to intubate, and they are more often difficult to position by nursing staff; they may also be harder to diagnose by imaging techniques. (D. Ryan et al, 2020)

Further, there is a complex interaction between obesity and the immune system. Obesity can impair the immune response to a viral infection. (Kass et al, 2020; Malavazos et al, 2020) Adipose tissue not only provides storage for lipids but it is considered an immune organ itself. (O'Rourke, 2009) Visceral fat produces a greater release of inflammatory cytokines, (Malavazos et al, 2020) with release of tumor necrosis factor (TNF)-alpha, Il-1 and Il-6, i.e., "aberrant cytokine activation" (P. Ryan and Caplice, 2020) or an "inflammatory shift." (O'Rourke, 2009) These are the same inflammatory cytokines released in a cytokine storm that viruses such as COVID-19 trigger.

The underlying factors that lead to inflammation in adipose tissue are not known; one hypothesis is that adipocytes enlarge with increasing obesity, with resultant hypoxia and even necrosis. (O'Rourke et al, 2020) Accumulated fat also induces oxidative stress through mechanisms such as chronic inflammation, and endothelial and mitochondrial dysfunction. (Costa de Lucena et al, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews,* 2020)

Obesity potentially affects every organ: it causes changes in the skin, lymph system, vascular system, and collagen structure: after surgery or trauma, there is more than a two-fold increase in infection in the blood, urinary tract, or respiratory systems, and obesity can affect wound healing. It can also affect the distribution of medication that can lead to under-dosing, including to a vaccine. (Huttunen and Syrjänen, 2013)

Felix Jenewein, Funeral procession for victims of the plague, 1901.
Source: Wellcome Trust Collection/Public Domain

Jar, "Fat Figure, 3rd-6th century, Moche civilization, Peru. Obesity is not a new disorder, but rates have continued to increase over the past 20 to 30 years worldwide, and no country has been successful in decreasing these rates.
Source: Metropolitan Museum of Art, NYC/Public Domain

Adipose tissue, as well, may act as a "reservoir" for greater spread of a virus and may enable prolonged viral shedding. (P. Ryan and Caplice, 2020) One mechanism for acute injury to the lungs with coronavirus is that the coronavirus binds with angiotensin converting enzyme 2 (ACE 2) for its intra-cellular invasion, and adipose tissue, itself, has higher levels of ACE 2. (Malavazos et al, 2020; Kassir, 2020; Moore and June, *Science,* 2020)

Obesity has considerable significant effects on a person's respiratory functioning, including to the lungs and chest wall. (Peters and Dixon, *Expert Reviews of Respiratory Medicine*, 2018) Visceral fat in the mediastinum and abdominal cavities as seen in obesity reduces respiratory compliance and contributes to symptoms of wheezing and dyspnea. (Peters and Dixon, 2018) An elevated BMI diminishes forced expiratory volume and forced vital capacity; these changes in "respiratory mechanics" affect the ability to maintain adequate oxygenation. (Hajifathalian et al, 2020) Obesity can lead to airway narrowing and to a "ventilation-perfusion mismatch." (Peters and Dixon, 2018) Further, mechanical dysfunction in the lungs seen in severe obesity may lead to more severe lower respiratory infections and even contribute to secondary infections, (Gao et al, *Diabetes Care*, 2020) as well as an increased risk of aspiration and pulmonary embolism after surgery.

Bottom line: Though there is much we still do not know about COVID-19, clinicians are finding that obesity itself, independent of other co-morbidities, makes COVID-19 patients, including at a younger age, more vulnerable for severe complications, such as prolonged hospitalization and the need for invasive mechanical ventilation.

Obesity is a chronic, low-grade state of inflammation and though it potentially affects every organ in the body, it has significant effects on the lungs, the initial primary target of COVID-19. With the two pandemics—obesity and COVID-19—rampant among the world's population, "...there are so many we shall have to mourn ..." For more discussion on COVID-19, please see my previous companion post, ***The Raging Cytokine Storm***.

About the Author

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