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Influenza pandemics, solar activity cycles, and vitamin D

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SUMMARY

There is historic evidence that influenza pandemics are associated with solar activity cycles (the Schwabe-cycle of about 11-years periodicity). The hypothesis is presented and developed that influenza pandemics are associated with solar control of vitamin D levels in humans which waxes and wanes in concert with solar cycle dependent ultraviolet radiation. It is proposed that this solar cycle dependence arises both directly from cyclic control of the amount of ultraviolet radiation as well as indirectly through cyclic control of atmospheric circulation and dynamics.

Introduction

In the 20th Century alone, there were three worldwide (pandemic) influenza outbreaks. These pandemics occurred in 1918, 1957, 1968 and represented 3 different antigenic subtypes of the influenza A virus: H1N1 (Spanish flu), H2N2 (Asian flu), and H3N2 (Hong Kong flu) [1]. A publication in this journal by Yeung hypothesized that historic influenza A pandemics were associated with solar activity cycles [2]. That publication presented evidence that major influenza outbreaks (including those of the 20th Century) were well correlated with the well-known Schwabe sunspot activity cycle. An explanation of these correlations alternative to that suggested by Yeung will be considered here: solar cycle induced vitamin D changes.

Historically, most interest in vitamin D had been relegated to its actions in calcium homeostasis and in bone formation. However, work over the past decades has revealed that vitamin D controls and/or ameliorates various pathologies. As will be discussed, arguments have been advanced that vitamin D also plays an important role in the morphology of influenza epidemics. As will be hypothesized here, changes in solar radiation induced vitamin D production in the human body over Schwabe-cycles account for the observed correlation of influenza pandemics with solar cycles.

Sunspot cycles and pandemic influenza outbreaks

There is a rich history of attempts to relate solar cycles to various human maladies. For example, statistically significant increases in myocardial infractions have been related to years of maximum solar activity [3]. The idea that influenza pandemics are related to solar activity cycles has been discussed in various publications [4,5]. A more recent quantitative consideration of this idea is contained in Yeung's 2006 article in Medical Hypotheses entitled "A hypothesis: Sunspot cycles may detect pandemic influenza A in 1700–2000 A.D." [2]. Using a binomial test it was found that historic reports of pandemic influenza A were associated with increased solar activity (using as its surrogate the International Sunspot Number – ISN). For seven pandemics over the interval 1700–2000 A.D. agreed upon by referenced historic reviews, the sensitivity of using sunspot numbers ISN > 50 for their detection was found to be 85.7% (95%CL = 59.8–100%, $p = 0.019$). Three major 20th influenza A pandemics (1918–1920, 1957–1958, and 1968–1969) were found to have ISN > 50. Use of a different sunspot classification system, the Group Sunspot Number (GSN) which is an upgrade of the ISN classification system, has been proposed to upgrade Yeung's analysis; but this would be expected to introduce changes in results only prior to year 1880 [6].

To explain these results Yeung suggested that the correlation of pandemics with Schwabe-cycles arose from solar cycle induced terrestrial climate changes on arrival times of migratory birds which facilitated genetic reassortment of circulating influenza viruses. An alternative explanation for the correlation will be offered and considered here: solar cycle induced vitamin D changes.

Vitamin D and influenza

Over the past three to four decades a revolution has occurred in our understanding of vitamin D and its effects. Sundry in vitro, animal, ecologic, and other human epidemiological, as well as some human studies have revealed that vitamin D generates positive and important responses in the immune, heart-cardiovascular, immune, muscle, pancreas, and brain systems, as well as positive involvement in ageing and control of the cell cycle and thus of cancer disease process [7]. Reasons have also been advanced which strongly suggest that vitamin D provides protection against

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low-level radiation damage [8], as well as exerting salutary control/amelioration of various maladies contributing to human ageing [9].

Drawing on the proposal of the late British epidemiologist Edgar Hope-Simpson that a "seasonal stimulus" intimately associated with solar radiation explained the remarkable seasonality of epidemic influenza, Cannell and associates proposed that wintertime vitamin D insufficiency explains seasonal variation in influenza and other viral respiratory tract infections [10,11]. They presented detailed arguments that adequate vitamin D levels play an important positive role in preventing and controlling respiratory tract infections. Their proposal is supported by prospective cohort [12] and case-control [13,14] studies which have demonstrated a consistent association between low levels of the major circulating metabolite of vitamin D (25[OH]D) and respiratory tract infections. These studies, although promising, were preliminary and based on only small, nondiverse patient cohorts. A recent large-scale observational study provided more substantial evidence. It involved the secondary analysis of the Third National Health and Nutrition Examination Survey (NHANES III) of about 19,000 Americans who had received physical and laboratory serum examinations and who were selected to be representative of the United States population. It showed an inverse association between (25[OH]D) and respiratory tract infections which was strongest in those with recent upper respiratory infections (the common cold) and chronic respiratory tract disorders such as asthma and emphysema [15].

Solar-induced vitamin D

While vitamin D can be taken in the diet, its primary source in the human population is solar ultraviolet B (UV-B) spectrum radiation induced skin synthesis [16]. Because more than 90% of vitamin D requirements for most people come from casual exposure to sunlight [17], lack of sunlight exposure is an important risk for vitamin D deficiency and such metabolic bone diseases as rickets, secondary hyperparathyroidism, and osteomalacia [18]. Altitude as well as season, time of day, and geographic latitude have been listed as important predictors of environmental UV-B radiation [19], and have been used as vitamin D surrogates in human ecological studies [20].

Factors affecting and observations of ultraviolet radiation at the earth's surface

The natural variation of ultraviolet (UV) radiation at the earth's surface is a consequence of the variation of atmospheric factors [ozone, clouds, aerosols (locally pronounced in strongly polluted areas, regionally in areas affected by smoke plumes from biomass burning or desert dust, and globally after volcanic eruptions), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and anthropogenic trace gases], geometric factors (solar zenith angle, earth–sun distance, altitude), and the ground's albedo. While the variation of the solar zenith angle and the earth–sun distance, primarily responsible for seasonal variations and their relationship with UV, are well established; most of the other factors need further study. The complicated spatial and temporal distributions of the variables that affect ultraviolet radiation limit the ability to describe surface radiation on the global scale, whether through measurements or model-based approaches. While many studies have demonstrated the inverse correlation between atmospheric ozone and ultraviolet radiation at the earth's surface, the detection of long-term ultraviolet trends is more problematic than the detection of ozone trends because in addition to its dependence on ozone, surface ultraviolet radiation is sensitive to clouds, aerosols, and surface albedo, all of which can exhibit large variability [21,22].

Under cloud-free skies, the most important atmospheric factors affecting surface UV radiation are stratospheric ozone, followed by tropospheric ozone and aerosols and, to a lesser extent, NO_2 and SO_2 and other trace gases in the atmosphere of urban areas [23]. (Outside the region affected by the Antarctic ozone hole, changes in ultraviolet radiation due to anthropogenic trace gases are rather small and are within the range of variability from other causes [24]). Changes in total atmospheric ozone are dominated by how much ozone is in the mid- to lower-stratosphere, with approximately ninety percent of the atmosphere's total ozone column being located in the stratosphere [25].

There are now relatively good long-term measurements of atmospheric ozone. While there have been re-constructions of UV radiation at the earth's surface by using radiative transfer and statistical models that use measured input parameters such as atmospheric ozone, global radiation, visibility, and clouds; the situation for long-term ground-based UV measurements are not as sanguine. Although the quality and quantity of surface UV measurements have increased in recent years, long-term measurements still only exist at a small number of locations and these few locations are unable to give a global picture of UV trends [26]. In addition, owing to the complexity of the instrumentation, high resolution UV spectrometers are notoriously difficult to calibrate and keep stable over long-term intervals [27]. While satellite UV data are available, they are as of yet usually of insufficient temporal length for present purposes. In addition, satellite-derived UV irradiance values are themselves problematic because they are based on backscattered UV. Detailed studies have demonstrated that satellite-based methods can seriously overestimate UV irradiance in the northern hemisphere, exceeding surface measurements by up to 40%. It has been suggested that this discrepancy arises because satellite-based methods require assumptions to be made about aerosol and tropospheric ozone extinctions in the lowermost region of the atmosphere (i.e., in the "boundary layer") which have proven to be error-prone [28].

Because of the dearth of reliable observational data on long-term surface ultraviolet temporal morphology, an alternative stratagem has oftentimes been employed to deduce UV changes over the Schwabe solar. This stratagem involves relating observed and deduced ozone change to UV changes by means of the Radiation Amplification Factor (RAF) which depends to first order on total ozone content of the atmosphere and solar height above horizon. For small changes in the ozone layer thickness, the wavelength-dependent RAF represents the percent increase in UV intensity for each 1% decrease in total column. For present purposes, the adopted RAFs are 1.25 for UV-B radiation, vis-à-vis 1.15 for erythemal UV radiation and 2.15 for DNA-weighted UV damage [29,30]. (Erythemally-weighted UV irradiance, i.e., skin-reddening or sunburn irradiance, has sometimes been adopted as a surrogate for UV-B irradiance.) This stratagem was employed Rozema et al. to deduce changes in DNA-weighted UV damage over solar cycles [31], with the cyclic DNA-damage results and not the germane UV-B results having been cited by Cannell et al. for influenza infectivity [10] and by Selas et al. for outbreaks of forest moth pest species [32]. Cited values of solar cycle ozone changes have varied, e.g., ranging from 3% to 7% for the upper stratosphere (at 35–45 km altitude) [33]. Adopting a value of 5% for stratosphere ozone solar cycle variability [34,35] yields an estimated concurrent 6.3% UV-B change.

Schwabe solar cycles and vitamin D control of influenza pandemics

The sun goes through an approximately 11-year cycle, the Schwabe-cycle (ranging from about 9 to 12 years), alternating between a quiescent state (with lower surface temperature) and an

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active one, with sunspots and a high surface temperature. It also has an approximately 22 year Hale cycle of solar magnetic polarity. Wavelengths in the range 100–400 nm constitute the solar ultraviolet spectral region. Stratospheric ozone is formed by solar UV-C radiation (100–280 nm), initially by photodissociating atmospheric molecular oxygen. While solar UV-C radiation does not penetrate as far as the earth's surface, Schwabe-cycle UV-C increases produce increased high-altitude ozone, which in turn absorbs more solar UV-B radiation (280–315 nm), with concomitant reductions in the amount of solar UV-B reaching the earth's surface. (Changes of solar UV-B per se over Schwabe-cycles are relatively minor: while UV-C irradiance increased by 2% during one recent solar cycle, the corresponding increase in solar (not surface) UV-B irradiance was only 0.4% [31].) Therefore counter-intuitively, solar UV-B received at the earth's surface is expected to be maximum at Schwabe-cycle solar output minimum; and vice versa, minimum surface UV-B is expected at Schwabe-cycle maximum.

Solar cycle activity is hypothesized to be related to influenza infectivity in the following manner. Maximum UV-B radiation and concurrent high vitamin D production levels occurring during solar cycle minimum provide prophylactic protection and promote immune system well being against influenza. Contrariwise, minimum UV-B radiation and concurrent low vitamin D production levels occurring during solar cycle maximum are detrimental by failure to promote adequate levels of prophylactic protection and immune system well being against influenza. These temporal modes of action are consistent with the fact that while influenza viruses are present in the population before pandemic occurrences [36], it is only during certain temporal intervals that they reach pandemic status. It is being proposed here that intervals of increasing and decreasing influenza infectivity are manifestations of solar cyclic control of vitamin D production.

Solar-induced stratospheric ozone changes are comparable to secular decreases (e.g., from increasing chlorofluorocarbon concentrations) and natural variations driven by oscillating equatorial stratospheric winds [37]. While atmospheric ozone changes have been associated with atmospheric dynamics and circulation, it is not obvious whether ozone changes are driving changes in dynamics and circulation or whether, vice versa, changes in dynamics and circulation are causing ozone changes. Nevertheless there is evidence that atmospheric ozone and concomitant UV-B are associated with modes of atmospheric circulation and dynamics modulated by the Schwabe solar cycle. These include the North Atlantic Oscillation (NAO), the Arctic Oscillation (AO) or Northern Annular Mode (NAM), and the Southern Annular Mode (SAM) [38,39]; as well as the Quasi-Biennial Oscillation (QBO) cycle, radiation belt energetic electron precipitation, and cosmic ray ozone depletion. The latter three processes merit further discussion here since each has been specifically associated with changes in atmospheric ozone and either directly or by inference associated with changes in ultraviolet radiation at the earth's surface.

Quasi-Biennial Oscillation (QBO) associated ozone and ultraviolet changes

The Quasi-Biennial Oscillation (QBO) cycle is a quasi-periodic oscillation between easterly and westerly zonal winds in the tropical stratosphere with a mean period of 28–29 months. The QBO is modulated by the Schwabe-cycle [40] and has been connected to ozone changes both in equatorial regions and at middle and even polar latitudes [41]. A detailed time series analysis for the Australian continent based on satellite ozone data associated significant changes in derived erythemal exposure to phases of the QBO and the solar activity cycle. It was suggested that enhancement in summer erythemal radiation exposure of about 10–20% above the climatological average might be expected in years in which the QBO is in its westerly phase and the solar cycle is at its minimum [42]. It has also been noted from satellite observations that the interannual variabilities of ozone and UV-B exposure driven by the QBO are larger than the decadal trends caused by the long-term loss of ozone at equatorial and middle latitudes (0° to about 50°) [43].

The amplitude of QBO erythemal dose derived from ozone satellite data was reported to be almost 40% of annual cycle amplitude in the tropics and decreases towards the extratropics, becoming less than 5% in middle latitudes [44]. This latitude decease arises from the fact that the mean amplitude of ozone seasonal changes is minimal in the equatorial zones and increases towards middle and high latitude, while the QBO has much smaller amplitude variation. The QBO peak-to-peak amplitude in erythemal dose derived from ozone satellite data was 6.5% at Thessaloniki, Greece. Previous ground-based measurements at that location showed that QBO variations were 8% of seasonal mean measured total ozone variations and 8.8% of seasonal mean measured erythemal dose variations [45].

Radiation belt energetic electron precipitation and ozone depletion

It has been proposed that precipitation of energetic electrons from the earth's radiation belts depletes mesospheric and stratospheric ozone [46]. This depletion has been attributed to downward transport from the mesosphere to the stratosphere of long-living nitrogen oxides (NO_x) produced through electron ionization. The electron flux has been cited as being closely related to the speed of the solar wind and showing a clear 11-year cycle with the maximum in the declining phase of the solar cycle. Analysis of balloon-borne ozone sonde and satellite measurements vis-à-vis atmospheric model calculations indicates the existence of winter polar ozone decreases of ≈20% which are strongly correlated with the flux of solar cycle modulated energetic electrons. Concomitant increase in surface UV-B radiation would be expected ca. the Schwabe-cycle minimum. There is evidence that high latitude ozone changes evince lower latitude ozone changes through changes in atmospheric dynamics and transport. It is known that ozone depletion in polar regions has an impact on the ozone depletion in mid-latitudes, with ozone-depleted air exported from polar latitudes comprising a significant portion of ozone losses at mid-latitudes [39]. For example, it has been shown that approximately 50% of the ozone depletion at mid-southern latitudes is attributable to the export of ozone-poor air from Antarctica [47], with evidence for enhanced UV-B radiation in Melbourne, Australia as a result of ozone-depleted air being transported from Antarctica [48,49].

Cosmic rays and ozone depletion

A clear relationship between galactic cosmic ray intensity and atmospheric ozone depletion has been reported over two full solar cycles spanning the interval 1980–2007, with maximum ozone depletion occurring at galactic cosmic ray maximum at Schwabe-cycle minimum (a manifestation of the Forbush cycle) [50]. This correlation was especially pronounced with polar ozone loss (hole) over Antarctica and was attributed to cosmic ray driven electron-induced reaction of halogenated molecules. The reported relationship between cosmic rays and ozone depletion shares similarities with the reports of energetic electron precipitation from the earth's radiation belts: maximum ozone depletion and concomitant expected surface UV-B radiation increases occur at Schwabe-cycle minimum and both invoke electrons as the deus ex machina.

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Conclusion

Arguments have been advanced in support of the hypothesis that influenza pandemics are intimately connected with solar cycle control of vitamin D levels in humans. As discussed, solar ultraviolet B (UV-B) radiation which is the main production source of vitamin D in humans waxes and wanes over the Schwabe solar cycles. It is proposed that maximum vitamin D production levels at the earth's surface which occur during solar cycle minimum would provide prophylactic protection and promote immune system well being against influenza. Contrariwise, it is proposed that minimum vitamin D production levels at the earth's surface which occur during solar cycle maximum would prove detrimental by failure to promote adequate levels of prophylactic protection and immune system well being. It is further proposed that changes in vitamin D levels, perhaps even of a relatively modest nature, could trigger factors important in controlling influenza infectivity.

As developed, vitamin D levels at the earth's surface arise both directly through solar cycle control of the amount of UV-B radiation, and indirectly through control of atmospheric circulation and dynamics with examples of the latter processes having been cited. Both the direct and indirect processes are important in support of the hypothesis being presented here: solar cyclic control of human vitamin D levels and influenza pandemics.

Conflict of interest statement

The author has no financial and personal relationships with other people or organizations that could inappropriately influence (bias) his work.

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