To Todd Flinn — Surrogate

FYI. We are working on passing your Greek/ The Religious Community Bill. We will work together. Best wishes to you. Pete.

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Clinton Presidential Records
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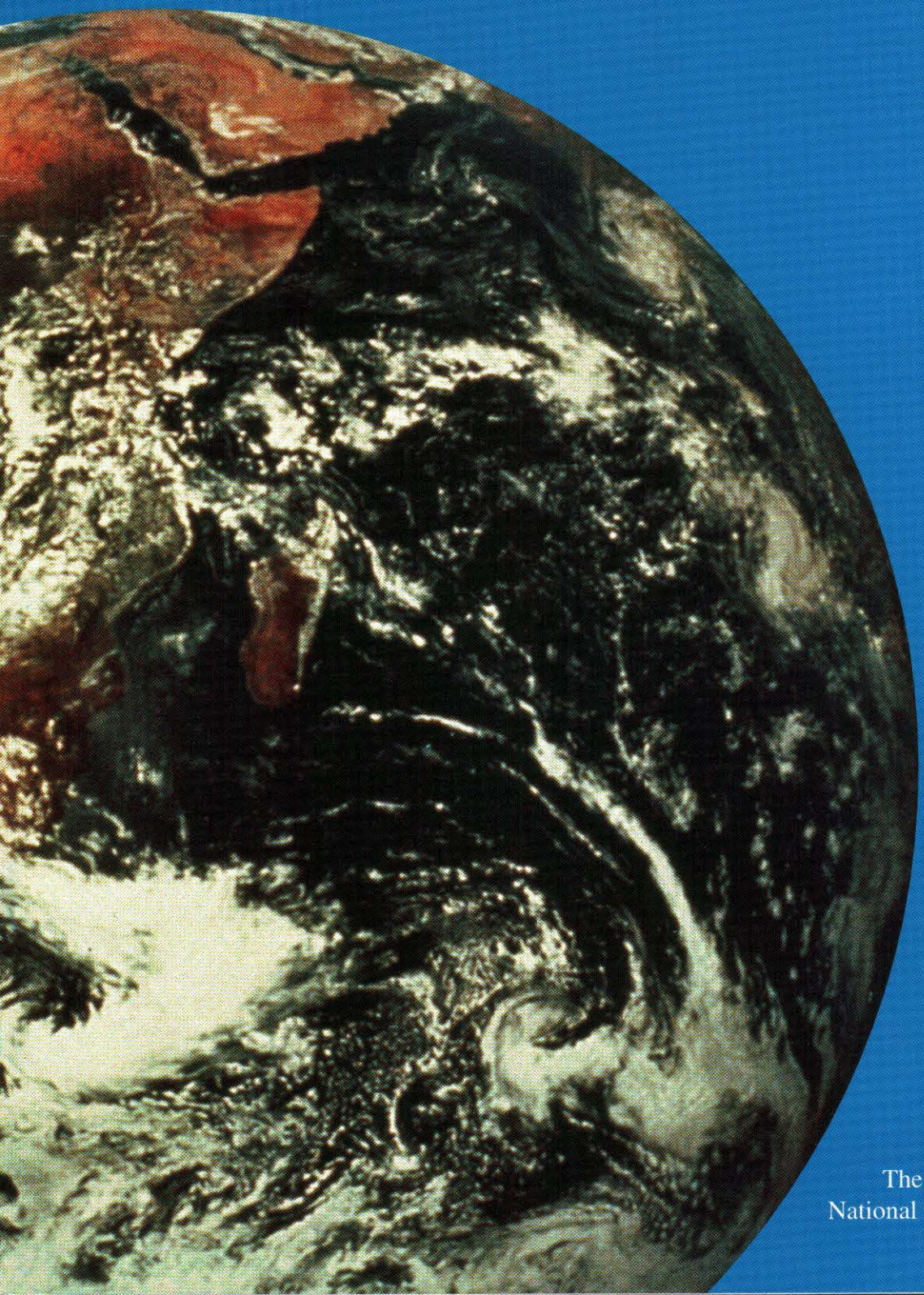
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It's God's World:
Christians, the Environment and Climate Change

A five session study for congregations by Vera K. White



Published by
The Eco-Justice Working Group
National Council of the Churches of Christ
in the USA

'97 JUL 25 PM1:01

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Jim Todd,

It was good speaking to you. I am interested in helping you, & the Administration in advancing its climate change policy proposals. Please feel free to call you me.

Jim Florio

B. Reid Detchon

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Memo

Henry Kelly OSTP

TO: Todd Stern

FROM: Reid Detchon

DATE: July 30, 1997

Energy and Bob Williams panel — BLAST Partnership

Overview

The Vice President has both a tremendous need and opportunity to show that his climate change objectives can be realized without major damage to the U.S. economy. Supporting the development of renewable energy alternatives to fossil fuels accomplishes this goal.

Of all those alternatives, the use of biomass energy is the least well understood by the public and has the most potential to contribute in the very near term. This means the conversion of organic material -- anything from farm and forestry wastes to dedicated energy crops -- to electricity and liquid transportation fuels (ethanol).

Technology development supported by the federal government for the past 20 years has put us in a position to rapidly expand the contribution that biomass can make and allow the U.S. to make progress toward its climate change objectives inexpensively by the year 2010.

This can be done by:

- Co-firing biomass with coal in existing utility boilers at a 10% ratio.
- Supporting the adoption of advanced cogeneration technology by the pulp and paper industry, which currently generates 7,000 megawatts of power from wood waste for its internal use.
- Demonstrating the conversion of biomass (other than corn) to ethanol -- for use as an alternative fuel in "flexible-fuel" vehicles, which Ford and Chrysler have already committed to mass-produce on a large scale. This can involve collaboration with the timber industry on the west coast and the agriculture sector in the Midwest and South -- with the acceptance of the environmental community.

The Office of Science and Technology Policy, through Henry Kelly, has had a Biomass Energy Initiative under development for quite some time. This proposal is consistent with, but not identical to, that initiative.

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Elements of a Biomass Energy Initiative

WHO: Vice President Gore

WHAT: Announce major new initiative in renewable energy, climate change

-- Forestry: Embrace Quincy Library Initiative (timber/environmental group collaborative)
- -- Forest Service will clear away unhealthy underforest growth
  - -- Creates more natural forest
  - -- Reduces fire risk, $1 billion cost of suppression
  - -- Enhances downstream water supply in California
  - -- New jobs in economically depressed area
- -- Convert to ethanol or power
  - -- Incentivize with low- or no-cost feedstock
  - -- Consider government role as cooperative partner

-- Transportation: Support first demonstrations of cellulose ethanol processes x5 feedstocks
- -- E.g.: Rice straw in CA, bagasse in LA, wood chips in CA/MN, switchgrass in AL, waste paper in NY
- -- Guarantee market for E-85 from cellulose
  - -- Federal fleets would be required to use in E-85 FFVs within reason
  - -- Extend ethanol tax incentive, possibly tailored to support cellulose

-- Agriculture: Apply Sec. 45 production tax credit to existing facilities, extend duration
- -- Would incentivize purpose-grown crops for co-firing

-- Power: Jawbone coal industry into co-firing
- -- Thousands of megawatts potential
- -- Will jump-start biomass supply business, provide experience in materials handling
- -- Instant CO2, SOx benefits
- -- Partner with pulp/paper industry on completion of Burlington gasification project, demonstration of commercial feasibility at scale (x3)
  - -- Potential 12,000 megawatts over next 10-20 years as boilers are replaced
  - -- Buy down risk through AFPA or equipment suppliers
    - -- Avoid corporate welfare charge

-- International: Emphasize opportunities for developing countries
- -- Renewable alternative to fossil fuels
- -- Domestic alternative to imported oil
  - -- Reduce importance of Persian Gulf
- -- Sustainable resource management creates net zero CO_2

WHEN: Before Kyoto

WHERE: Multiple locations, emphasizing different aspects (e.g., California re Quincy)

WHY:

-- Politically: Wide geographic base would benefit
(Agriculture, Midwest/South;
Forest, Pacific Rim, New England, Southeast, Midwest North)
-- Environmental support, esp. acid rain states (reduced sulfur from co-firing)
-- Little adverse reaction likely
-- Gore needs to show action on climate change without cost

-- Environmentally: Substantive action on climate change without disrupting existing economy (as per Byrd resolution)
-- Closed carbon cycle
-- Only renewable transportation option
-- Suitable for developing nations
-- Additional environmental benefits from perennial energy crops
-- Acid rain reductions from co-firing
-- Forest health improvement from better management
-- Resolves waste disposal problems for biomass residues (e.g., rice straw)

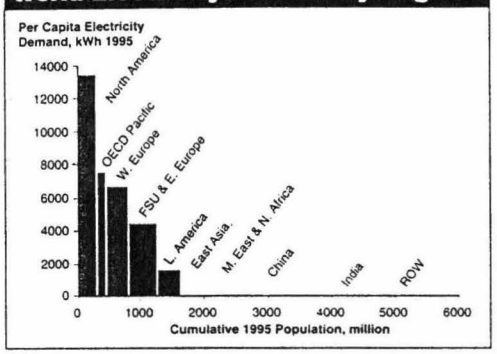
-- Economically: Least-cost approach to large-scale introduction of renewables
-- Cofiring, pulp/paper retrofit can occur at minimal cost
-- Green marketing may support more costly renewable power
-- Rural economic development, jobs from gathering, processing biomass
-- Reduced oil imports means reduced trade deficit
-- Technologies may be exportable

-- Energy: Only near-term answer to oil import dependence
-- Reduced national security threat
-- FFVs are making the market ready
-- Only near-term renewable baseload power option
-- Can work alongside coal
-- Utility restructuring is creating consumer choice
-- Identify biomass as a green option

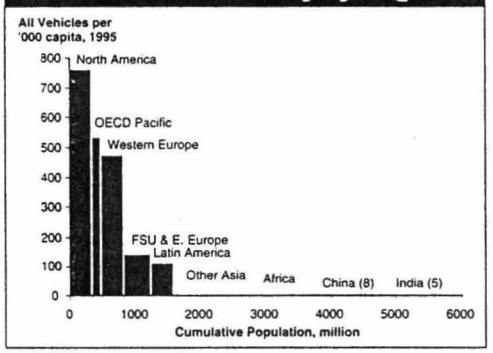
The Evolution of the World's Energy Systems

Over the last hundred years, energy demand per capita has more than trebled, from 3 to 13 boe/year, spurred by economic growth. However, major parts of the world's population have still little or no access to the comfort provided by electricity nor to the wider range of choices and opportunities linked to mobility. Meeting these needs, for today and tomorrow, will require increased and sustainable energy supplies. To reflect on this challenge, a study of the evolution of the world's energy system was conducted in 1994 in Shell Group Planning by Georges Dupont-Roc, Alexon Khor and Chris Anastasi. Extracts are presented in this paper.

World Electricity Demand by Regions



World Vehicle Density by Region



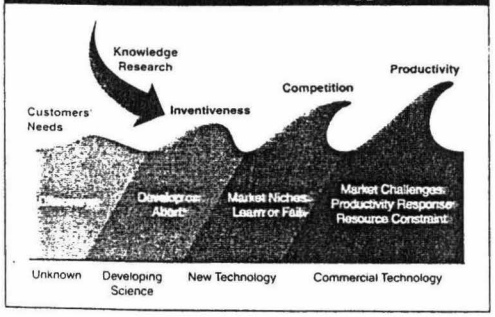
Against the background of a world population growing from 5 billion people today to 8.5 billion by 2030, and stabilising at 10 - 12 billion by 2060, as envisaged by the World Bank, what energy system could sustainably fuel a continuing world economic growth of 3% per annum, similar to that experienced over the last hundred years?

Building on historical patterns which have shaped economic development - inventiveness, competition, productivity, converging developments - two contrasted energy visions are explored for the future.

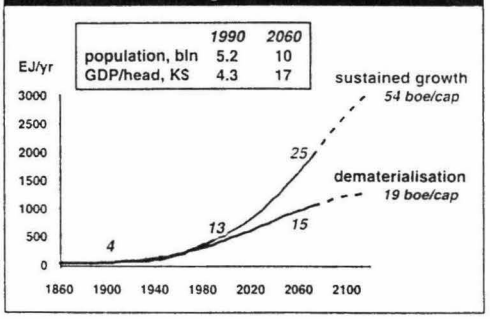
- In "Sustained Growth", abundant energy supply is provided at competitive prices, as productivity in supply keeps improving in an open market context. The growth pattern of the last century continues, with energy consumption per capita reaching 25 boe/yr by 2060, today's Japanese level.
- In "Dematerialisation", human needs are met through technologies and systems requiring a much lower energy input. A different pattern emerges, leading to an energy use per capita of 15 boe/yr by 2060.

For both scenarios, fossil fuels contribute to most of the growth over the next few decades, but renewable energy sources gradually take an increasing market share and their contribution becomes significant by 2020-2030. The Group is currently undertaking a small number of demonstration projects, focused on testing the commercial potential of biomass - growing trees for heat and power generation - and photovoltaics systems.

Waves of Technology



Two Simple Scenarios



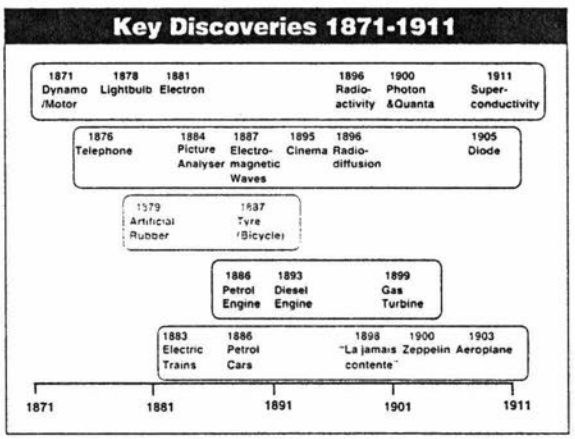
What have we learnt so far?

Key discoveries made 100 years ago have shaped today's life

Their history shows:

- Vigorously pursued concepts, like television;
- Surprises: it took some thirty years to understand the significance of radioactivity;
- Competitive development, like Zeppelin versus Aeroplane or petrol versus electric cars. For instance,
  "La jamais contente", an aluminium bodied and battery powered car, broke the speed record at 105 km/h in 1899 but never made it to the market.

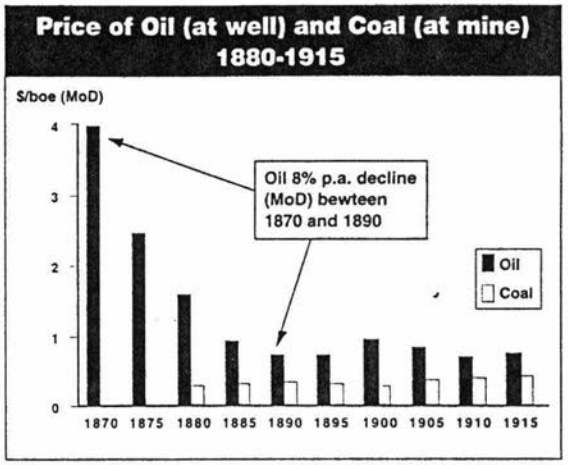
Against this promising background, mankind was using mostly wood and coal to meet its energy needs. By 1890, oil market share was only 2%.



Oil came into the energy market through niches

Oil was first used in lamps and stoves. As industry learnt how to produce it, the average price decreased at a rate of 8% p.a. over 20 years and a 50 fold production increase was achieved from 1870 to 1910. Used increasingly in commercial ships, it became an established player when Sir Winston Churchill switched the British Navy from coal to oil, gaining a strategic advantage from increased power and less visible smoke emissions. By then, the oil price was in real terms close to today's level.

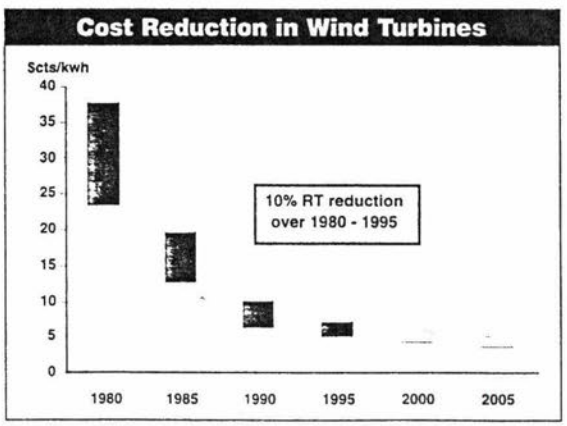
In the 1970s, sharp increases in oil prices led oil companies to develop resources at the upper end of the cost curve. When prices collapsed in the mid 1980s, competitive pressures forced engineers in the oil industry to stretch their imagination to propose competitive technologies.



For instance, Troll - an oil and gas field offshore Norway, in some 300m water depth, declared commercial in 1983 - saw its capacity cost reduced by 7% p.a in real terms over 1983-1993. This trend can also be shown for many North Sea projects after 1985 and led to the development of completely new technologies and practices which have now become routine – sub-sea satellites, unmanned platforms, long range deviated wells.

Today, several renewable energy technologies are following a similar path down their learning curves

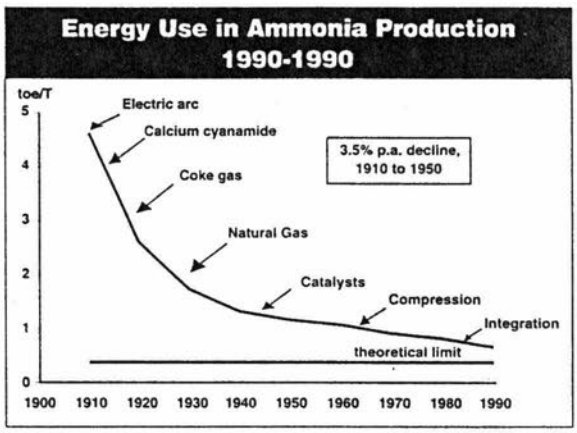
The cost of electricity from wind turbines fell by 10% p.a. in real terms over 1980 - 1995. Although based on an intermittent source, this technology is now commercially competitive in certain areas. This happened through improved reliability, optimising design, location and economy of scale in manufacturing and stimulated by "pump priming" policies of certain governments. There are now a dozen major manufacturers and a new industry is emerging.



Between 1976 and 1988, the cost of making photovoltaic solar panels steadily declined at rates in excess of 15% p.a. in real terms, following an 80% experience curve (costs are reduced by 20% when the cumulative number of installations doubles).

Productivity also improved in the use of energy

There are many examples in industry. For example, the energy used in the industrial production of ammonia has seen a steady decline over an extended period of time through the adoption of new raw materials, processes and equipment. Today, only one-fifth of the energy required in 1910 is needed.



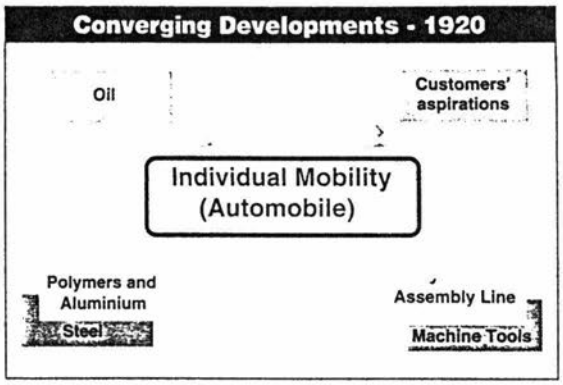
In transport, very high speed trains, such as the French TGV, fulfil the same need as their steam ancestor but faster and using less primary energy. The weight per passenger remains an area of potential improvement.

This process of continuous improvement is reflected at macro economic level. In the USA, energy intensity - the ratio of energy consumption to gross domestic product - has declined at an average of 1% p.a. over the last 100 years, with up to 2% p.a being achieved for a decade under extreme price pressure.

In the history of economic development, there are times when converging needs and resources can radically change life-style

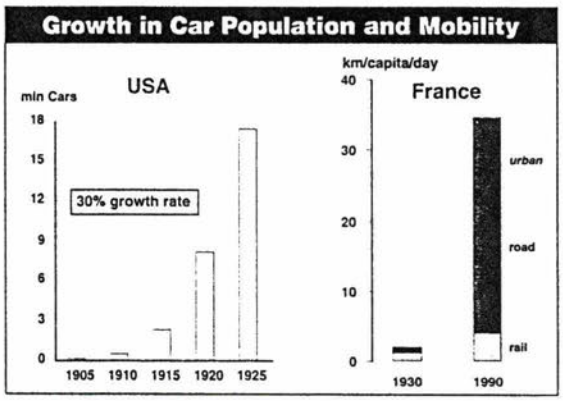
For instance, individual mobility came about from the convergence of:

- A new energy source (oil with its high energy density);
- Improved and new materials (quality steel, polymers);
- New manufacturing techniques (assembly line production);
- Social needs, such as wider choices for dwelling, working and leisure.



Mass produced cars became affordable to many, growing, in the USA, from 8000 in 1900 to 17 million in 1925 -a sustained growth of 30% p.a.

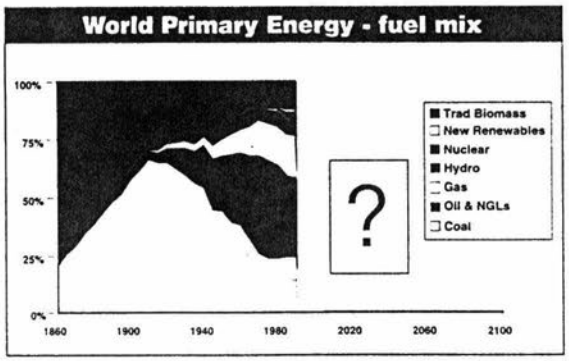
John Watkins speculated in "The Ladies' Home Journal" of December 1900 that "automobiles will soon become cheaper than horses and be substituted for every horse vehicle now known ... including police patrols"



As demand grew, energy supplies became more diversified

As new needs appeared and economic development progressed, energy demand grew and consumption per capita in the world kept increasing over the last century, even during troubled periods. To meet these needs, energy supplies became more diversified:

- coal, oil, gas, hydro, nuclear.....and we may now be seeing the beginning of a new transition: - new renewables.



Waves of technological transitions will continue this process

One generation will make a discovery, perhaps explain the science and teach it to the next generation which, in turn, will develop it and bring it to our daily life. This process may take 40 to 60 years. Along this path inventions may abort or fail to become commercial. For some of the more robust, "pump priming" through limited grants may be needed to facilitate the progression along the learning curve through market niches.

Identified renewables - wind, biomass and solar photovoltaics - are clearly new technologies looking for market niches. Artificial photosynthesis and magma energy are at the stage of developing science. There are many other candidates and the unknown will no doubt bring "surprises".

"Sustained Growth"

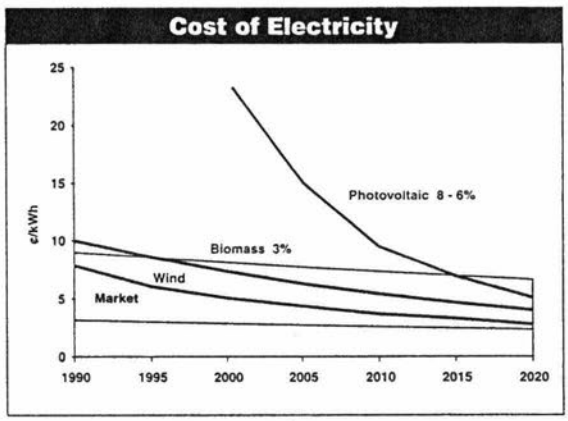
Abundant energy supply is provided at competitive prices, as productivity in supply keeps improving, in an open market context

Companies and universities active in the deployment of renewable energy technologies would be successful, stimulated by limited "pump priming" initiatives. This would occur not only in OECD countries, but also in developing countries. As a result, the challenge of providing abundant energy at competitive prices would be met over the next decades.

New technologies would steadily progress along their learning curves, first capturing niche markets and, by 2020 become fully competitive with conventional energy sources. Cost reductions reflect an 80% experience curve for solar photovoltaics and 85 % for biomass. This is not unlike the progression of oil 100 years ago (80%) and slower than that of electricity in the USA between 1926 and 1970 which followed a 75% experience curve (a 25% cost reduction for every doubling of cumulative production).

The cost of sustainably growing biomass could be reduced by advances in clonal propagation and genetic enhancement of plants, notably woody crops. Conversion, first into electricity, and later into liquid fuels, could become commercial through small scale replicable facilities. Over the last decade, Shell companies have developed experience in growing and enhancing trees (for pulp wood) and are now becoming involved in the development of biomass (trees) for heat and power generation.

The cost of photovoltaic panels would be reduced, first by advanced automation in manufacturing and improved light conversion efficiency in current crystalline silicon technology. It could be followed by the large scale deployment of one or several types of thin film technologies. A Shell company has recently developed an improved high efficiency cell, in cooperation with public research organisations and will implement industrial production.

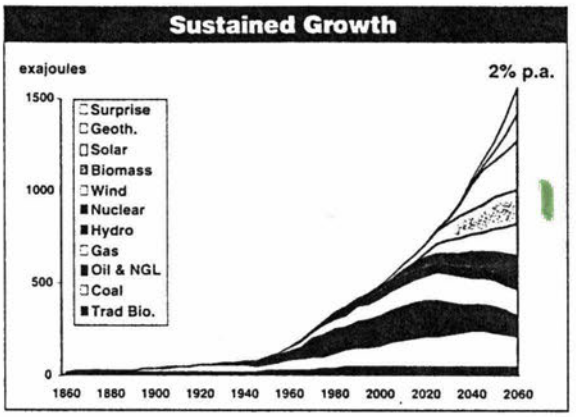


Renewable energy sources become significant by 2020

An attempt is made here to illustrate what energy supply could look like under "Sustained Growth". Primary energy grows at about 2%, supporting a 3% p.a. growth in GDP. This assumes an improvement in energy intensity of about 1 % p.a. as observed in the USA between 1880 and 1990, under free market conditions. Energy per capita continues its historical progression.

Use of fossil fuels increases steadily over the next 30 years, fuelling the economic development of a majority of the world population. By 2020-2030, they reach their maximum potential and no longer contribute to growth, being limited by the rate of production and commercialisation of resources

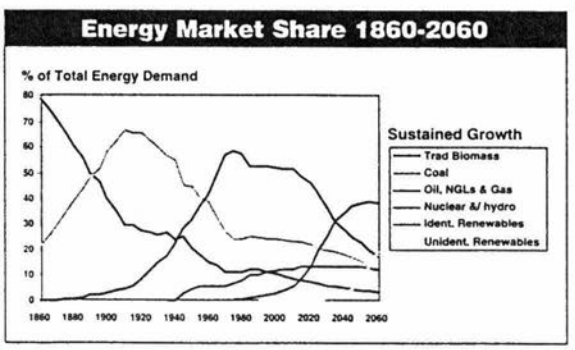
economically competitive with renewable energies. At that time a number of developing countries (e.g. China and India) - having reached a sufficient level of industrial development - increasingly turn their attention towards renewable energy sources. Some of them may be able to leapfrog, as illustrated by rapid growth of wind power in Asia-Pacific countries and India.



Having gradually become commercial over the next two decades, renewable energy technologies increase their market share as total energy demand grows. This allows growth in energy supplies to be sustained at a time when fossil fuels reach a plateau. It is not necessary, for this argument, to determine which renewable technology has the best prospects. Technologies will compete but the market will decide.

However, by 2060, sources of supply are likely to be more diversified than today. Perhaps ten different sources will each have a market share between 5 and 15%.

In this scenario, the rate of market penetration for identified renewable technologies - wind, biomass, photovoltaics - is similar to that of coal or oil and gas in the past. A second wave, possibly including magma energy and/or a surprise, might take-off by 2050.



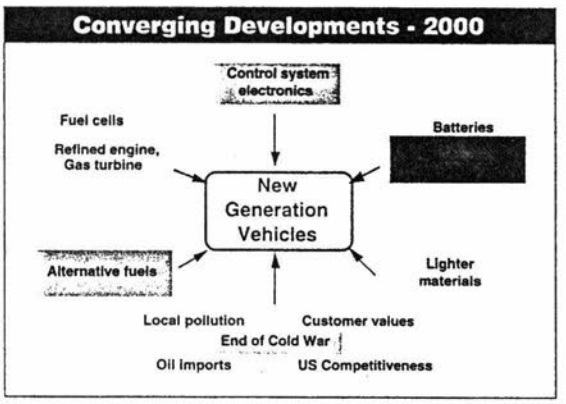
"Dematerialisation"

Human needs are met through technologies and systems requiring a much lower energy input

For instance, data highways and virtual reality may be a harbinger of a different lifestyle, a signal perhaps similar to the emergence of the automobile and individual mobility at the beginning of this century.

Thanks to advances in materials and design capabilities, objects and equipment will fulfil their function using ever less or lighter material. Carbon fibres are four times lighter than steel and yet twice as strong.

Certainly in road transport one could see a possible convergence of social and economic issues, new technologies - some of them developed for space application - alternative fuels and lighter materials. The result would be "New Generation Vehicles", three times more fuel efficient than today's vehicles. The challenge is to integrate these technologies, lower their cost and develop a manufacturing infrastructure, probably along an evolutionary path.



"... new technologies, such as advanced electronics, ultra light materials, CAD and a host of others could change cars more radically in the next 10 to 20 years than in the last 100"

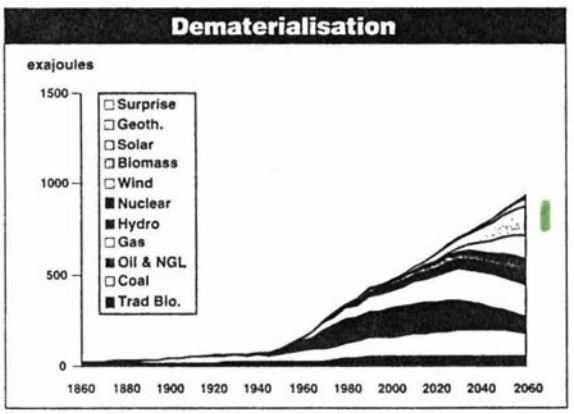
A. Trotman, Chairman of Ford Motor Co.

Energy consumption per capita remains virtually stable for the next 30 years

An attempt is made here to illustrate what energy supply would be consistent with "Dematerialisation". Improvement in energy intensity gradually reaches a sustained 2% p.a. To support a 3% p.a. growth in GDP, primary energy increases at about 1.3% p.a. until 2030, as developing economies expand. Thereafter, energy growth slows down to 1% p.a., as "Dematerialisation", started in the more advanced regions of OECD countries, gradually spreads to industrialising and developing countries, once infrastructure has been built and GDP per capita is high enough. Countries restructuring their economies would improve their energy efficiencies drastically.

Coal and oil growth is lower in "Dematerialisation" than in "Sustained Growth". However, more gas is being used to compensate for the delayed take-off of PV solar, postponed from 2020 to 2050. This technology remains a niche application until nanotechnology becomes widely applicable!

A 2% p.a improvement in energy intensity has only been seen for limited periods in the past. In "Dematerialisation", relentless advances in information technology, telecommunication, materials and biotechnology would enable high energy intensity improvements to be sustained for several decades.

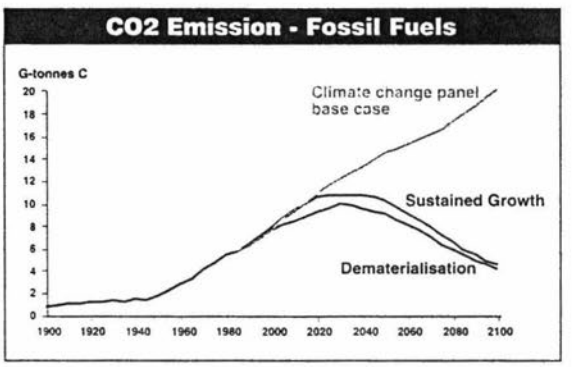


A different life style, possibly linked to changing individuals' and customers' behaviour, could emerge. Signs may already be perceivable such as virtual reality, but consequences are difficult to anticipate fully, perhaps similar to the scale of changes brought about by the automobile and individual mobility during the 20th century.

In "Dematerialisation", the rate of market penetration for identified renewable energy - wind, biomass, PV solar - is lower than in "Sustained Growth". The second wave of renewables is not needed until 2060.

Conclusions

- Hydrocarbons are needed for economic development
- Productivity improvement in supply and use will continue
- Energy needs will be met by more diverse sources
- "Carbon free" newcomers can become competitive through market mechanisms. Markets will decide which technology is best.
- CO2 emissions from fossil fuels peak at around 10 GtC before the middle of the next century and decline to 4GtC/year by 2100, leading to stabilisation of CO2 content in the atmosphere at about 550 - 600 ppm, according to current models, or 60% above today's level.



Among many different possible paths along which the world energy system could develop, "Sustained Growth" and "Dematerialisation" are two sustainable and plausible archetypes which could happen through market mechanisms and with minimum stimulation. These scenarios provide low economic cost options to policy makers and are genuinely "no regret".

Like 100 years ago, there are many talents in the world. Provided governments maintain a framework in which inventiveness, competition and productivity are encouraged and rewarded and where decisions are the result of a rational and open debate, business can do a lot to support sustained economic growth, supplying and using energy in an environmentally responsible manner.

WHAT MAY HAPPEN IN THE NEXT HUNDRED YEARS

By John Elfreth Watkins, JR.

Extracts from Ladies' Home Journal - December 1900

America with Five Hundred Million People. There will probably be from 350,000,000 to 500,000,000 people in America and its possessions by the lapse of another century.

Hot and Cold Air from Spigots. Hot or Cold air will be turned on from spigots to regulate the temperature of a house as we now turn on hot or cold water from spigots to regulate the temperature of the bath. Central plants will supply this cool air and heat to city houses in the same way as now our gas or electricity is furnished. Rising early to build the furnace fire will be a task of the olden times. Homes will have no chimneys, because no smoke will be created within their walls.

Trains One Hundred and Fifty Miles an Hour. Trains will run two miles a minute, normally; express trains one hundred and fifty miles an hour. To go from New York to San Francisco will take a day and a night by fast express. There will be cigar-shaped electric locomotives hauling long trains of cars. Cars will, like houses, be artificially cooled.

Everybody will Walk Ten Miles. Gymnastics will begin in the nursery, where toys and games will be designed to strengthen the muscles. It will be compulsory in the public schools. Every school, college and community will have a complete gymnasium. All cities will have public gymnasiums. A man or woman unable to walk ten miles at a stretch be be regarded as a weakling.

There will be No C, X or Q in our every-day alphabet. They will be abandoned because unnecessary. Spelling by sound will have been adopted, first by the newspapers. English will be a language of condensed words expressing condensed ideas, and will be more extensively spoken than any other. Russian will rank second.

Automobiles will be Cheaper than Horses are To-Day. Farmers will own automobile hay-wagons, automobile truck-wagons, ploughs, harrows and hay-rakes. A one-pound motor in one of these vehicles will do the work of a pair of horses or more. Children will ride in automobile sleighs in winter. Automobiles will have been substituted for every horse vehicle now known. There will be, as already exist to-day, automobile hearses, automobile police patrols, automobile ambulances, automobile street sweepers. The horse in harness will be as scarce, if, indeed, not even scarcer, than as the yoked ox is to-day.

Ready-Cooked Meals will be Bought from establishments similar to our bakeries of to-day. They will purchase materials in tremendous wholesale quantities and sell the cooked foods at a price much lower than the cost of individual cooking. Food will be served hot or cold to

Man will see Around the World. Persons and things of all kinds will be brought within focus of cameras connected electronically with screens at opposite ends of circuits, thousands of miles at a span. American audiences in their theatres will view upon huge curtains before them the coronations of kings in Europe or the progress of battles in the Orient. The instrument bringing these distant scenes to the very doors of people will be connected with a giant telephone apparatus transmitting each incidental sound in its appropriate place. Thus the guns of a distant battle will be heard to boom when seen to blaze, and thus the lips of a remote actor or singer will be heard to utter words or music when seen to move.

Telephones Around the World. Wireless telephone and telegraph circuits will span the world. A husband in the middle of the Atlantic will be able to converse with his wife sitting in her boudoir in Chicago. We will be able to telephone to China quite as readily as we now talk from New York to Brooklyn. By an automatic signal they will connect with any circuit in their locality without the intervention of a "hello girl."

Photographs will be Telegraphed from any Distance. If there be a battle in China a hundred years hence snap-shots of its most striking events will be published in the newspapers an hour later. Even to-day photographs are being telegraphed over short distances. Photographs will reproduce all of Nature's colors.

Grand Opera will be Telephoned to private homes, and will sound as harmonious as though enjoyed from a theatre box. Automatic instruments reproducing original airs exactly will bring the best music to the families of the untalented. Great musicians gathered in one inclosure in New York will, by manipulating electric keys, produce at the same time music from instruments arranged in theatres or halls in San Francisco or New Orleans, for instance.

The American will be Taller by from one to two inches. His increase in stature will result from better health, due to vast reforms in medicine, sanitation, food and athletics. He will live fifty years instead of thirty-five as at present - for he will reside in the suburbs. The city house will practically be no more. Building in blocks will be illegal. The trip from suburban home to office will require a few minutes only. A penny will pay the fare.

Coal Will Not be Used for Heating or Cooking. It will be scarce, but not entirely exhausted. The earth's hard coal will last until the year 2050 or 2100; its soft-coal mines have become more and more expensive. Man will have found electricity manufactured by water-power to be much cheaper. Every river or creek with any suitable fall will be equipped with water-motors, turning dynamos, making electricity. Along the seacoast will be numerous reservoirs continually filled by waves and tides washing in. Out of these the water will be constantly falling over revolving wheels. All of our restless waters, fresh and salt, will thus be harnessed to do the work which Niagara is doing to-day: making electricity for heat, light and fuel.

There will be Air-Ships, but they will not successfully compete with surface land and water vessels for passenger or freight traffic. They will be maintained as deadly war-vessels by all military nations. Some will transport men and goods. Others will be used by scientists making observations at great heights above the earth.

Peas as Large as Beets. Peas and beans will be as large as beets are to-day. Sugar cane will produce twice as much sugar as the sugar beet now does. Cane will once more be the chief source of our sugar supply. The milk-weed will have been developed into a rubber plant. Cheap native rubber will be harvested by machinery all over this country. Plants will be made proof against disease microbes as readily as man is to-day against small-pox. Soil will be kept enriched by plants which take their nutrition from the air and give fertility to the earth.

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March 1997

TO: Interested Parties

FR: Scott Sklar
Executive Director
National BioEnergy Industries Association (NBIA)

RE: Options Paper: International Sustainable Biomass CoFiring Initiative: G-7 Meeting (June 1997) pre-Kyoto Goal

---

Executive Summary

The World Resources Study "A New Power Base: renewable Energy Policies for the Nineties and Beyond" released in 1994 stated that biomass power contributed 3.1 quads of energy in the U.S. in 1990 but the economically accessible resource is 14 quads per year. The 1992 study released by Johansson, Kelly, Reddy and Williams as fodder for the 1992 UN Global Warming meeting in Rio noted that biomass energy accounted for 14.7 percent of the world's energy and that nearly 10 percent of world energy use could be sustainably harvested from crop, forest and manure residues or 31.2 exajoules of a total 373 exajoules worldwide. The study further stated that if sustainable biomass was grown on plantations, the potential would be 266.9 exajoules, or in other words, our planet could rely on sustainable biomass energy for its primary energy supply.

The Johansson et. al study is bolstered by the Royal Dutch Shell analysis cited in the April 1996 Atlantic Monthly cover story which cites that renewable resources will account for half of the world's energy by 2040 and biomass will be the largest renewable energy component. According to an April 1992 Congressional Office of Technology Assessment Study "Fueling Development: Energy Technologies for Developing Countries", 35 percent of the developing world's energy comes from biomass, mostly inefficiently. Bringing on more efficient technologies could more than double the energy output of biomass energy where 65 percent of the world's population resides.

In the late, Maheshwar Dayal's 1989 book "Renewable Energy: Environment & Development", the former Secretary of India's Department of Non-Conventional Energy laid out one of the most important aspects of bioenergy for the developing world -- energy plantations are an important contribution towards poverty alleviation and improvement of the 2 billion+ rural poor. Sustainable biomass plantations would employ 150 people per day for 1000 hectares of fast-growing trees and an additional 650 people over the year per 4,000 hectares for waste fuel wood. Dayal goes further to state that sustainable biomass projects could truly stabilize rural-to-urban migration by proving in-situ, stable employment. The fact was reiterated by Francisco Gutierrez, the Executive Secretary of OLADE, the energy ministerial group of Latin America who stated at the 1994 Enercon Conference speech, "the most important step to dramatically improve the environment is to alleviate poverty" particularly in rural areas where one-third of the planet's population lives, in poverty.

And in a 1994 World Bank Study, "Renewable Energy Technologies: A Review of the Status and Costs of Selected Technologies" authored by Kulsum Ahmed, the study shows that biomass-electric generation facilities over 20 megawatts could drop from $1,599 (US) per kilowatt hour to $870 (US) per kilowatt hour by the year 2000 with advanced biomass integrated gasifiers tied to steam-injected turbines. According to the Washington-based National Biomass Industries Association (NBIA), both the aforementioned technology and others including whole tree energy and advanced biomass cofiring with coal could achieve the $700 - $850 (US) per kilowatt hour cost thresholds in near term maturity.

ISSUE#1: If Biomass can be sustainably planted and utilized, what is the barrier?

Simply, coal is still the baseload electric power of choice for the developing world and transportation of biomass is the single greatest barrier in the developing world, not technology. Unless there is some new approach to build the biomass transportation infrastructure, market penetration will be underwhelming.

ISSUE #2: If the big eight countries: Brazil, India, Indonesia, Mexico, Peoples Republic of China, Russia and The Ukraine, South Africa, and The Philippines move rapidly towards coal generation, little other actions by any other countries could compensate in regard to greenhouse gas emissions.

Simply, some new approach is needed to supplant coal (and simultaneously sequester carbon) in those countries, using economic incentives appears to be the only realistic option.

THE PROPOSAL

The basic approach supports sustainable biomass cofiring with coal in which any country that voluntarily agrees to cofire sustainable biomass (replanted in an environmentally-sound way) at the 15 percent level per coal generation facility would be paid the difference of utilizing biomass coal cofiring via the World Bank's Global Environmental Facility (GEF).

The rational for such an approach is fourfold:

1) This approach insures that those countries moving inexorably towards coal generation would be compensated incrementally so that they would not lose money moving in this preferred sustainable biomass cofiring direction

2) This approach guarantees private sector-supported carbon sequestration utilizing fast-growing biomass which will be maintained and rotated to insure carbon sequestration is sustainable. Only fast-growing biomass sequesters the most carbon though certain biomass wastes which also degrade into greenhouse gases could be transitionally used until the fast-growing biomass matures (i.e. rice hulls). Developing nation governments routinely use soldiers to guard its biomass resources which will inevitably become old-growth forest rather than sustainable carbon-sequesters.

3) This approach will fundamentally develop the transportation and planting infrastructure necessary to make biomass a usable resource at the levels necessary to become a dominant fuel resource.

4) Cofiring is a known technology and the U.S. is the global leader with Europe and Japan also having leading technology. By incrementally hybridizing existing power plants as they are being built, the financial system will more easier acclimate to this new approach utilizing existing technology.

COFIRING: THE PREFERRED ENVIRONMENTAL ANSWER.

The World Coal December 1996 article on the environmental benefits of cofiring use primarily data from the Tennessee Valley Authority and four coal cofiring facilities in the following states Dunkirk, NY (90 MW), Dresden, N.Y. (104 MW), York Haven, PA (1,322 MW) and Portland, PA (1,200 MW). Aside from significant carbon and sulfur oxide reduction, annual fuel savings ranged from $108,000 to $680,000 per facility.

The Tennessee Valley Authority data using eastern and western coal, wood and 15% wood and 5% tyre-derived fuel with coal registered the following reductions:

Ultimate Analysis	Eastern Coal	Western Coal	Wood	Wood Co-firing 15%
Carbon	68.6	66.91	28.5	61.85
Sulfur	2.24	0.58	0.05	0.57
Chlorine	0.24	<.01	<.01	0
Ash	8.26	7.33	3.7	6.66

But the minimum 15 percent (which could be higher offsets) coal by 15 percent and emissions by 15 percent or greater, is truly valuable when you review the carbon sequestration data which is shown in the chart below developed in 1995 by Oak Ridge National Laboratory:

LABORATORY UPDATE: OAK RIDGE NATIONAL LABORATORY

FIGURE 2

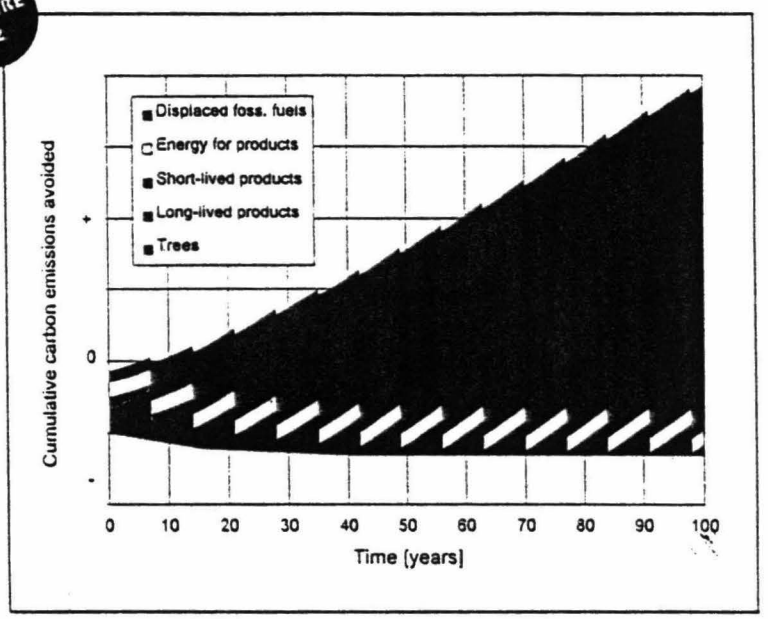


Figure 2: When a productive forest is harvested and the site replanted with energy crops, the initial harvest will yield some long-lived products, some short-lived products, and some energy products. Over time, the various products will gradually decay and release their carbon to the atmosphere and some carbon will be lost from the soil because of more intensive management. The energy products harvested periodically over time will displace fossil fuels, allowing them to be left in the ground. There will also be some fossil fuels left unburned because wood products typically require less energy for their production than do other materials for which they substitute. The cumulative reduction in carbon emissions over time will depend on the rate of energy-crop growth, the efficiency of biomass substitution for fossil fuels, and many other parameters being modeled in studies at ORNL and Joanneum Research. The carbon balance would look much different (better) if this scenario were implemented on surplus agricultural land because we would expect a buildup of soil carbon and no loss of carbon to the atmosphere as wood products are oxidized over time.

No other electric technology exists which not only can easily supplant coal generation using existing power plant technology AND sequester carbon at the same time. The elegance of incremental coal offsets while creating an institutionalized carbon storage process using the private sector is the critical attribute of the sustainable biomass cofiring approach.

The core issue to announce a plan would be the financing package and sunset the support because the market, itself, can takeover. Most experts agree that if twenty-five newly-built coal generation plants in the nine aforementioned countries used sustainable biomass cofiring in the next five years, the global market penetration would be enough to sustain itself.

To achieve that ambitious goal, the OECD governments would have to announce agreement in the short-term that the following multilateral lending and grant programs would be leveraged for both sustainable biomass resource planting as well as payments for the incremental capital cost "delta":

- Global Environmental Facility (The World Bank) both for biomass planting and certain facility support

- International Finance Corporation utilizing an accelerated window approach

- Multilateral Investment Fund of the InterAmerican Development Bank and a corollary program at the Asian Development Bank which would create an accelerated window, a set-aside capital pool, and longer term amoritization of the cofiring part of the loan

- Enhance existing sustainable energy programs (i.e. Solar Project of The World Bank, Sustainable Market for Sustainable Energy of the InterAmerican Development Bank) as well as UNDP for preinvestment project support in an accelerated delivery format

The OECD meeting would have to announce consensus on the sustainable cofiring option targeted to the potential "big coal" user countries and accelerated use of existing multilateral grant and lending programs as the primary delivery vehicle for investment tied to timetables so that the multilateral lending bureaucracy will delay.

If this announcement could be achieved with cooperation by the multilateral lending agencies using their existing programs, it is likely that sustainable biomass cofiring projects would be announced in 1998.

Follow-up activities would also be required which would include briefing engineering and investment firms tied to the coal and biomass industries since they are the first tier in coal plant design and operations. Technical briefing programs hosted by OECD countries such as the U.S. regarding TVA and other existing cofiring projects.

Project tracking using the multilateral lending institutions as well as existing NGO's such as E & Co (founded by the Rockefeller Foundation) to insure project status and barriers are quickly tracked and understood.

Multilateral bank industry briefing sessions to the global industry using specialized brochures and forms regarding program criteria and financing options.

Multilateral bank country briefings, of the nine targeted countries, so they are clear what they must do to make these funds available to their potential coal projects to meet "greenhouse gas emissions" goals.

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FAST FACTS ON BIOMASS ENERGY

More electric power is produced from biomass than any other renewable energy resource except hydropower. More than two-thirds of U.S. non-hydro renewable generation comes from biomass. This does not show up in some data because the power is almost all produced for on-site consumption by pulp and paper mills using wood waste.

What is biomass? It is plant material -- lignocellulose -- which can be used to produce electric power or converted into liquid transportation fuels. Examples include: sawdust and other wood waste; agricultural waste such as corn fiber, rice straw, or bagasse (pulped sugar cane); and the organic component of solid waste -- paper trash and yard clippings.

The U.S. has enough agricultural land available to produce enormous quantities of biomass in a sustainable way -- enough, for example, to replace half of our gasoline usage, or our nuclear power, twice over. Development of a biomass energy industry would be a multibillion-dollar shot in the arm for the rural economy, creating jobs and investment.

Federal support for R&D has moved these technologies dramatically down the cost curve -- e.g., reducing the cost of ethanol from biomass from $4 a gallon to $1 or less. The critical need now is to support first-of-a-kind demonstrations to accelerate commercialization.

Power:

We have invested $50 billion over the last 20 years on nuclear energy R&D. That's enough to fund the biomass power budget for the next 1,500 years.

The fusion budget is more than 10 times larger than the biomass power budget. Yet a commercial fusion plant is at least 50 years away. Biomass power technology is moving to market today, and the DOE budget supports that commercialization process.

One very promising immediate application involves co-firing with coal. Niagara Mohawk is preparing to demonstrate the production and use of fast-growing willows in western New York as a feedstock for power. This will reduce sulfur and other emissions and open up a vast market.

Fuels:

The budget request for developing transportation fuels is $40 million. We spend that amount on imported oil every 6 hours -- four times a day.

If this tiny investment in an alternative to imported oil can reduce the trade deficit and help the economy even a fraction, we will be repaid many times over.

Again, the DOE budget request supports entry into the marketplace, and it should be fully funded.

Biomass Energy Facts for the House Renewable Energy Caucus

1)
Biomass is the "secret" renewable. More electric power is produced from biomass than any other renewable resource except hydropower. More than two-thirds of U.S. non-hydro renewable generation comes from biomass -- almost all produced for on-site consumption by pulp and paper mills using wood waste.

2)
What is biomass? It is plant material -- lignocellulose -- which can be used to produce electric power or converted into liquid transportation fuels. Examples include: sawdust and other wood waste; agricultural residues such as corn fiber, rice and wheat straw, or bagasse (pulped sugar cane); and the organic component of solid waste -- paper trash and yard clippings. The U.S. has enough agricultural land available to produce enormous quantities of biomass in a sustainable way -- enough for example, to replace half our gasoline usage, or twice the amount of electricity that we now get from nuclear power.

3)
Penny-wise and pound foolish?

- We have invested $50 billion over the past 20 years on nuclear energy R&D. That's enough to fund the biomass power budget for the next 1,500 years.

- The nuclear fusion budget is more than 10 times larger than the biomass power budget. Yet a commercial fusion plant is at least 50 years away. Biomass power technology is moving to the market today.

- The R&D budget for developing transportation fuels is $40 million. We spend that amount on imported oil every 6 hours -- four times a day.

4)
Development of a biomass energy industry would be a multibillion-dollar shot in the arm for the rural economy, creating jobs and investment. Because biomass is bulky to transport, conversion facilities will be built where the biomass is grown. The USDA estimates that 17,000 jobs will be created for every 1 billion gallons of ethanol produced. The Electric Power Research Institute (EPRI) estimates that 5 quads of electricity generated from energy crops grown on 50 million acres would boost total farm income by $12 billion per annum.

5)
The use of biomass for energy will greatly reduce the Nation's greenhouse gas emissions. The use of fossil fuel removes carbon that is stored underground and releases it in the atmosphere. In a combustion system, biomass releases carbon dioxide as it burns, but biomass needs that same CO2 to grow -- thus creating a closed carbon cycle. In addition, significant quantities of carbon can be captured in the soil through biomass root structures, creating a net carbon sink. With the prospect of binding emission agreements, this is a solution that is here and ready today.

6)
Agricultural land that would otherwise be converted to residential or industrial use -- as we need fewer acres to meet the market demand for food -- can be used to grow biomass crops that restore soil carbon, reduce erosion and chemical runoff, and enhance wildlife habitat. Perennial energy crops are the same kinds of crops we now plant to protect fragile lands under the Conservation Reserve Program. They can be harvested without damage to the root structure and thus continue to serve as a soil stabilizer and stream buffer and habitat for wildlife.

THE WHITE HOUSE

WASHINGTON

Surrogates

Thank You

INTERFACE

'97 JUL 24 AM 10:15

Ray C. Anderson
Chairman and Chief Executive Officer

July 21, 1997

Mr. Todd Stern
Staff Secretary and Assistant to the President
Old Executive Office Building
Room 180
Washington, DC 20502

Dear Todd:

It was a pleasure for me to meet you last week, as part of the President's Council on Sustainable Development (PCSD) and the PCSD's Climate Change Task Force.

I don't envy you the task you have been handed by the President, but it's clear that you are a very thoughtful person and a quick study. I hope the PCSD can help you in the huge task that lies ahead.

The PCSD is made up of competent and trustworthy people who are there because they care, and not for any other reason. Marty Spitzer has, by now, given you a list of the initiatives we believe we can launch and manage. We stand ready and willing to help.

All the best.

Sincerely,

RCA/kg

cc: Jonathan Lash
Marty Spitzer
Dr. James Baker
Steve Percy
Christine Ervin

Interface, Inc. 2859 Paces Ferry Road, Suite 2000 Atlanta, Georgia 30339 770.437.6801 770.437.6822 fax



INTERFACE





Mr. Todd Stern
Staff Secretary and Assistant to the President
Old Executive Office Building
Room 180
Washington, DC 20502

SURROGATE LIST NEEDS:

1. Revise chart format.

It would be helpful to divide into the following main categories:

- Science (need to include atleast those from recent event);
- Business (need to include small, medium, large, various industries and technologies);
- Environment;
- International;
- Labor;
- Government (local, congress, Governors);
- Former Officials;
- Bipartisan; and
- Administration.)

Helpful sub-categories would include:

- Name;
- Title;
- Organization;
- Area of Expertise;
- Phone;
- Fax;
- Press or Executive Assistant Name,
- Assistant's Phone (preferably work and home),
- Region or State (where they live, work or where organization is strong),
- Current Effort (this should include if they attended WH meeting or event, signed the Science letter, already participate in surrogate effort);
- Strength (speeches, print, radio, television).

2. Priority list for each main category.

3. Draft script for calling through potential surrogate list.

United States Department of the Interior

OFFICE OF THE DEPUTY SECRETARY
Washington, D.C. 20240

'97 AUG 5 PM 4:43

August 1, 1997

Mr. Todd Stern
The White House
Ground Floor, West Wing
Washington, D.C. 20500

Dear Todd:

As you can see from the enclosed letter from former Governor Florio, he wants to help us on the climate change issue. I have talked to him and he is very committed to the issue and reasonable resolutions.

Is there any way that he could be of assistance to you and the President?

Sincerely,

John Garamendi
Deputy Secretary

Enclosure
cc: James J. Florio

FLORIO & PERRUCCI, P.C.

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June 18, 1997

John Garamendi, Deputy Secretary
U.S. Department of the Interior
1849 C Street, N.W., Room 5110
Washington, D.C. 20240

Dear Mr. Secretary:

Thank you very much for taking the time to meet with me. I enjoyed our discussion, and was particularly pleased to talk with your Chief of Staff, Chantale Wong.

I am interested in being of some assistance to you and Secretary Babbitt, and feel that by virtue of my background in the field of environmental and energy policy, that that might be the most useful area to explore. The global warming initiatives that have been launched by the Administration, represent an area of interest for me, and I will follow through in contacting some of the individuals that you suggested that I talk to in the various agencies that are helping to frame the Administration's policy.

If there are other ways in which you feel that I can be of assistance to you and Secretary Babbitt, please feel free to call upon me. Again, thank you for your courtesy.

Sincerely yours,

James J. Florio

JJF:pon

cc: Chantale Y. M. Wong
Chief of Staff to the Deputy Secretary

UNITED STATES
DEPARTMENT OF THE INTERIOR
OFFICE OF THE SECRETARY
WASHINGTON, DC 20240

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Mr. Todd Stern
The White House
Ground Floor, West Wing
Washington, D.C. 20500

United States Department of the Interior

OFFICE OF THE DEPUTY SECRETARY
Washington, D.C. 20240

'97 AUG 6 AM8:55

August 1, 1997

Mr. Todd Stern
The White House
Ground Floor, West Wing
Washington, D.C. 20500

Dear Todd:

Dr. Paul Epstein is a terrific resource on the health effects of global warming. He wants to be helpful.

Sincerely,

John Garamendi
Deputy Secretary

Enclosure
cc: Paul R. Epstein, MD, MPH

CENTER FOR HEALTH AND THE GLOBAL ENVIRONMENT
HARVARD MEDICAL SCHOOL

May 19, 1997

John Garamendi
Deputy Secretary
United States Department of Interior
Washington, DC 20240

Dear John,

It was a pleasure to meet you in March when I spoke at the Department of State luncheon on the health implications of climate change.

I am writing to ask for your suggestions on how to follow up and bring greater attention to these connections. Additionally, I wonder if I might trouble you to write a brief letter concerning my presentation, that would be used for seeking further foundation support for our Center for Health and the Global Environment at Harvard Medical School.

Most importantly, I look forward to exploring with you how health concerns can be better integrated into the broad range of issues including land management and biodiversity, as well as policies concerning climate change.

I enclose a recent book chapter and other articles dealing with these connections.

With best regards,

Paul R. Epstein, MD, MPH

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CHAPTER 1

Global Environmental Degradation and Biodiversity Loss: Implications for Human Health

ERIC CHIVIAN

> "The Planet is not in jeopardy. We are in jeopardy. We haven't got the power to destroy the planet—or to save it. But we might have the power to save ourselves."
>
> —Michael Crichton, *Jurassic Park* (1990)

Introduction

There is abundant evidence that we are beginning to alter, for the first time in history, the chemistry and physics and physiology of the Earth. A basic understanding of biological systems and their dependence on the environment should alert people to the potential dangers these alterations pose for human beings. Yet, most people, including most policymakers, do not comprehend the human implications of global environmental change. Underlying this lack of comprehension is the widespread belief that human beings are separate from the environments in which they live, that they can change the atmosphere and oceans—and damage marine, aquatic, and terrestrial ecosystems in the process—without these changes affecting them.

In focusing on the human health dimensions of biodiversity loss, this volume helps people understand that human beings are an integral part of the environment, and that to protect their health and lives, and those of their children, people must learn to protect the environment.

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Biodiversity and Human Health

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This chapter will provide an overview about how environmental degradation leads to biodiversity loss, and what the implications of this loss are for human beings. This is an enormously complex topic, one that is in its infancy in terms of scientific understanding. Much of what can be said about it is uncertain and speculative. But the subject is also perhaps the most important one of all—namely the ways that global ecosystems support human health and make human life possible, and there is enough evidence available in the scientific and medical literature to justify looking at possible future scenarios, especially as they may serve as warnings.

Medicine brings a new perspective to discussions about global environmental change. It has a long tradition of acting decisively to prevent life threatening situations from occurring even when all the evidence is not in. The low threshold for performing appendectomies is a case in point (Gross 1956)—if surgeons waited until they were absolutely certain that their patients had appendicitis, it would often be too late to prevent serious illness and death. This is the situation we face today with global environmental degradation. If we wait until we have definite proof of its occurrence and of its consequences, it may be too late to avoid a medical catastrophe.

This chapter will cover the contributions to biodiversity loss from:

- global climate change,
- stratospheric ozone depletion,
- toxic substances in the environment, and
- habitat destruction;

and the possible effects on human health from this loss, including:

- the loss of medicines,
- the loss of medical models, and
- the emergence and spread of infectious diseases.

Central to these discussions will be two themes:

1. That the study of species and biodiversity may be the best means we have for recognizing future danger signals to human health from global environmental degradation, as some species may be so uniquely sensitive to specific assaults on the environment that they may serve as our "canaries," or so-called "indicator species."

2. That we must focus much greater attention on biodiversity loss, which looms as a slowly evolving, potential medical emergency of unprecented proportions, still largely unappreciated by policymakers and public.

When *Homo sapiens* evolved, some 100,000 years ago, the number of species on Earth was the largest ever, but current rates of species extinction resulting from human activities, at least 1000 times those that would have occurred naturally, rivalling the great geologic extinctions of the past, may be reducing these numbers to the lowest levels since the end of the Age of Dinosaurs, 65 million years ago (Wilson 1993). Paul Ehrlich and E.O. Wilson (1991) and others have predicted that one-quarter of all species now alive may become extinct during the next 50 years if these rates of extinction continue.

There are 100 times more people on Earth than any land animal of comparable size that ever lived, and we are the most voracious and destructive species that ever existed. We consume or destroy or co-opt, for example, as much as 40% of all the solar energy trapped by land plants (Ehrlich and Wilson 1991). Not only is this behavior morally indefensible, endangering in the process countless other species, it is fundamentally and ultimately self-destructive.

Several aspects of global environmental degradation have an impact on species populations and biodiversity. This chapter will briefly review some of the evidence.

Global Climate Change

The Intergovernmental Panel on Climate Change (IPCC), the United Nations working group of 2500 of some of the world's most eminent atmospheric, physical, and biological scientists, has stated that projected worldwide CO_2 (the main greenhouse gas) emissions will result in an increase in global mean surface temperatures of about 1.8 to 6.3°F by the year 2100 (IPCC 1995). The magnitude of these changes may not seem very large, but it must be remembered that the difference between the temperatures at present and those at the peak of the last ice age, 18,000 years ago, are only 5–9°F (Stevens 9/20/94), and that temperatures of 7°F higher than those of today have not been present since the Eemian interglacial period 130,000 years ago (Stevens 11/1/94), and perhaps not since the Eocene epoch, tens of millions of years ago (Webb 1992).

Even small changes in temperature can lead to enormous changes in global weather patterns and habitats. For example, during the years from about 1000 to 1350 A.D., known as the "Medieval Warm Period," when global mean surface temperatures were only slightly more than 1°F warmer than they are now, there were vineyards in England, and Greenland supported hundreds of farms (Ponting 1991). By contrast, from 1430

to 1850, the period known as the "Little Ice Age," when global mean surface temperatures were only slightly more than 1°F cooler than they are now, the Thames was often frozen in winter, and there were icebergs off the coast of Norway (Leggett 1990).

Since the late 19th century, global mean surface temperatures have already warmed on average approximately 1°F (Stevens 1995), consistent with the increases in atmospheric CO_2 concentrations during the past century, from preindustrial revolution levels of 280 ppm to current levels of 350 ppm (Maskell et al. 1993). And 1995 was the warmest year since 1856, when mean global temperatures were first systematically recorded (Stevens 1996).

There is growing evidence that the seas are undergoing a similar warming, from measurements off the coast of California (Barry et al. 1995) and deep in the Atlantic Ocean (Parrilla et al. 1994), and that sea levels worldwide have risen about 10–20 cm over the last century (Warwick and Oerlemans 1990). The IPCC predicts that with greenhouse warming, sea levels will increase an additional 15–95 cm by the year 2100 (IPCC 1995).

These predicted changes in climate and sea levels will pose enormous and unprecedented threats to plant, microbial, and animal species, including human beings.

Many paleontologists believe that climate change, both global warming and cooling, was the dominant factor in the great extinctions of the past (Eldredge 1991), both directly, because of shifts in temperature outside the ranges to which species could adapt, and indirectly because of changes in habitats, for example, the formation of glaciers or changes in sea levels (Stanley 1987). Fossil records indicate that many species have been able to adapt to climate changes by shifting their ranges—during warming periods, for example, species colonized new habitats nearer the poles or at higher altitudes, while during cooling periods they retreated back toward the equator (Peters and Darling 1985). During several Pleistocene interglacial periods, when mean surface temperatures in North America were 3–5°F higher than they are at present, Cape Cod had forests like those found in present day North Carolina, manatees swam off the coast of New Jersey, and osage oranges grew near Toronto, several hundred kilometers north of their present ranges (Peters and Darling 1985). But many other species could not adapt and were lost, either because their rates of migration were too slow, or because geographical barriers like oceans, mountains, or unsuitable habitat conditions prevented their advance (Peters and Darling 1985).

By contrast to the past major changes in climate, however, when temperatures warmed or cooled over thousands of years, the changes predicted

over the next century will be an order of magnitude or more faster, and it is not at all clear, even if there were no barriers to migration, whether species can migrate fast enough to avoid extinction. But there *are* barriers everywhere people live—cities, roads, agricultural lands, and other human constructions would further complicate species migration. It is calculated, for example, that for each 1°C rise in temperature, land plants would have to shift their ranges toward the poles by 100–150 km (Roberts 1989). The warming predicted by 2100, for example, would mean shifts of a few hundred kilometers. Some species, propagated by spores or dust seeds, might be able to achieve these rates (Perring 1965); most others would not (Peters and Darling 1985). Some spruce tree species, for example, even though they have light, wind-carried seeds, disperse them no farther than 200 m from the parent tree, corresponding to a potential maximum migration rate of only 20 km per century (Seddon 1971).

Animals, while more mobile, would be limited by the distributions of the plants they eat or otherwise depend on, by their ability to adapt behaviors to climate-altered habitats, or by changes in the populations of their predators or competitors, even if they could adapt physiologically (Peters and Darling 1985).

We may already be seeing evidence of species migrations and potential losses, paralleling the increases in recorded temperatures—in large reductions in red spruce trees in New Hampshire over the last 200 years (Hamburg and Cogbill 1988), in the upward climb of several vascular plant species in the Austrian alps over the past 70–90 years (Grabherr et al. 1994), in the shift to the north of Edith's checkerspot butterfly in the western United States (Parmesan 1996), and in the dramatic shift northward of a large number of marine invertebrate species off the coast of California over the past 60 years (Barry et al. 1995). In one particularly alarming study, warming seas off the coast of San Diego have been linked to an 80% reduction in zooplankton since 1951 and to similar declines in sea birds and fish, with the creation of a veritable "biological wasteland" (Roemmich and McGowan 1995).

Other aspects of global climate change that could have major impacts on species and biodiversity include: algal blooms (fertilized by the discharge of sewage and by agricultural run-off) (Epstein and Colwell 1993); rising seas that may threaten species in coastal wetlands, mangrove swamps, and coral reefs (Grigg and Epp 1989); the very worrisome possibility of major alterations of ocean currents from sea warming and changes in salinity, with potentially enormous changes in climate and in marine ecosystems (Broecker 1987); and finally the increase in CO_2 itself, which may threaten ecosystems by altering carbon and nitrogen cycles fundamental to the in-

teractions between plants, the atmosphere, and the soil (Hilchey 1993) [for example, by slowing photosynthesis in some land plants (Korner and Arnone 1992)]. Furthermore, global warming may increase turnover in tropical forests, favoring rapidly growing, light-demanding plants (that take up less CO_2) over denser, slower-growing, shade-tolerant plants (Phillips and Gentry 1994), thereby accelerating global warming (Pimm and Sugden 1994).

If one considers the human species as a part of biodiversity, it is clear that greenhouse gas warming will also eventually reduce human numbers, as human beings are exquisitely sensitive to high temperatures (Rogot and Padgett 1976, Kilbourne 1992, Kalkstein 1993). During the two-week summer heat wave in the eastern United States in July 1993, for example, 84 people died in Philadelphia as a result of the increased temperatures (*Morbidity and Mortality Weekly Reports* 1993). And during the five days in mid-July 1995 when temperatures over 100°F swept over the central plains of the United States, there were 700 excess heat–related deaths in Chicago alone (*Morbidity and Mortality Weekly Reports* 1995, Semenza et al. 1996, Kellermann and Todd 1996).

The indirect effects on human health secondary to global climate change—from infectious diseases caused by a spread of disease vectors (Shope 1991) or by changes in habitats [resulting, for example, in outbreaks of cholera (Epstein 1995)]; from crop failure; from violent weather patterns; and from the unavailability of drinking water—are likely to extract an even heavier toll on human beings.

With global climate change, we are clearly conducting a gigantic experiment with life on this planet, knowing almost nothing about the potential consequences, endangering perhaps not only countless microbial, plant, and animal species, but ultimately perhaps ourselves as well. No human subjects committee at any hospital or medical research facility would ever approve this experiment to be performed.

Stratospheric Ozone Depletion

Stratospheric ozone depletion may also threaten species, both on land and in the sea. It was the formation of the ozone layer 450 million years ago that permitted marine life forms to colonize the land, as it protected them from the lethal effects of ultraviolet radiation.

In the mid 1970s Mario Molina and Sherwood Rowland (1974) predicted that the continued use of chlorofluorocarbons (CFCs) would lead to a decrease in stratospheric ozone, but it was not until 1985 that the first

conclusive evidence of ozone depletion was reported (Farman et al. 1985), when ozone levels over the Antarctic were observed to have declined by 40% between 1975 and 1984 compared to 1960 baseline levels. Since then, record low levels have been recorded over the Antarctic in 1993 [down by more than 70% (Wilford 1993)], and over the Arctic in 1995, when readings 40% below normal values were recorded (Zurer 1995). Significant ozone depletion has also been observed by NASA and NOAA scientists over the heavily populated middle latitudes of the Northern Hemisphere, with early 1993 levels down by 10 to 20% (*New York Times* 4/23/93), and with corresponding increases in ground level ultraviolet-B radiation (UV-B) (Kerr and McElroy 1993).

The increased UV-B reaching the ground as a result of ozone thinning will damage the DNA and proteins of all living things (Leaf 1993), and could become a cause of species extinction and of a loss of biodiversity. Food crops (Worrest and Caldwell 1986), wild plants, and marine phytoplankton (Bridigare 1989) may all be affected, with possible major implications for terrestrial and marine food chains. Animals would also be vulnerable. Laboratory studies have shown, for example, that UV-B can lead to suppression of the immune response in mice, rats, and guinea pigs (Kripke 1990). Some amphibians seem particularly sensitive (see below), and there are anecdotal reports of sheep developing cataracts in Punta Arenas, Chile, at the tip of South America, beneath the ozone "hole" (Sims 1995).

Again, human beings are also at substantial risk, with increased rates expected of nonmelanocytic skin cancers (Suarez-Varela et al. 1992), malignant melanomas (Kricker et al. 1994), and cataracts (Taylor et al. 1988). The incidence of malignant melanomas has been increasing faster than that of any other cancer in the United States and worldwide (Rigel 1994), growing in Western populations by 20 to 50% every five years over the past two decades, particularly in young adults (Coleman et al. 1993). Every 11% decrease in stratospheric ozone is expected to increase melanoma mortality by 0.8 to 1.5% (Hoffman and Longstreth 1987).

Of great concern also is the potential for UV-B to weaken the systemic immune response in humans (Kripke 1990, Jeevan and Kripke 1993), potentially impairing peoples' ability to fight infections and cancers.

Toxic Pollution

Toxic substances—air pollutants such as acid rain, nitrogen dioxide, and ground level ozone; long-lived chlorinated hydrocarbons such as DDT and

polychlorinated biphenyls (PCBs); heavy metals such as lead, mercury, cadmium, copper, arsenic, and molybdenum; and other compounds that alter immune, endocrine, or reproductive systems—may also act to threaten species and reduce biodiversity. The enormous quantities of such substances released into the environment [in the United States in 1988, 0.36 billion pounds of toxic chemicals, for example, were released into lakes, rivers, and streams, 2.43 billion pounds into the air, and 0.56 billion pounds into landfills (U.S. EPA 1990)] coupled with the almost complete absence of toxicity information available for the tens of thousands of chemicals in current use (National Research Council 1984) make this an area of enormous research importance.

There are several mechanisms by which toxic substances may be harmful to those organisms exposed.

Airborne Pollutants

The emission of air pollutants high into the atmosphere, particularly by fossil fuel burning power plants, results in the formation of acidic aerosols [mostly sulfuric acid, metallic acids, and ammonium sulfates (Christiani 1993)], and the eventual deposition of these as acid rain or snow. There is good evidence that this acidic precipitation may reduce biodiversity in terrestrial ecosystems, for example, in freshwater habitats (Hutchinson and Havas 1980, Altshuller and Linhurst 1983, Blaustein et al. 1994). The complexity of the effects of such acidification on ecosystems can be seen in two recently studied examples. In one study acid deposition, when combined with climate warming, was shown to increase the penetration of UV-B radiation in freshwater ecosystems, exposing aquatic organisms at greater depths to harmful radiation (Schindler et al. 1996). In another, the spreading of lime in southwest Sweden, which was done since the mid 1980s to counteract the effects of acidification from power plants and factories, has been thought to have caused the death of hundreds of moose in that region (Line 1996). The deaths seem to have been the result of increased concentrations of the element molybdenum, secondary to the liming, in plants eaten by the moose, leading to an imbalance between molybdenum and copper in the moose livers and a resultant fatal copper deficiency in the animals.

Other forms of air pollution, such as ground level ozone, produced mainly by the combustion of gasoline in motor vehicles, can also be toxic to various life forms, including food crops (Brown and Young 1990) and

some forest trees (Prinz 1987, McLaughlin and Downing 1995). And the role of heavy metals (carried by polluted air) in the decline of forests has only recently begun to be elucidated (Gawel et al. 1996).

Endocrine-Mimicking Substances

In 1991, twenty-one biologists met in Racine, Wisconsin, to share observations about a wide variety of amphibians, reptiles, birds, and some marine and land mammals that demonstrated endocrine and reproductive effects, thought to be caused by exposure to synthetic chemicals in the environment (Colborn and Clement 1992). A sense of urgency was expressed at this and subsequent meetings, as it was believed by those attending that some chemical pollutants mimicked hormone activity in these animals, and by doing so, disrupted embryonic development and reproductive functioning. The result, they believed, was an observable decline in many North American species (Colborn and Clement 1992).

There was also great concern that these effects could occur in humans (Colborn et al. 1993, Colborn et al. 1996), and that the increased incidences of breast and prostatic cancers in the United States between 1969 and 1986 (Hoel et al. 1992, Davis et al. 1993, Davis and Bradlow 1995), the 400% increase in U.S. ectopic pregnancies between 1970 and 1987 (Nederlof et al. 1990), the marked rise in the incidence of cryptorchidism (undescended testes) (Chilvers et al. 1984) and hypospadias (a malformation of the penis where the urethra opens on the underside) (Matlai and Beral 1985) in the United Kingdom over the past 20 years, and the decline in sperm counts (Carlsen et al. 1992, Auger et al. 1995) and in normal sperm [with lower percentages of motile and morphologically normal sperm (Auger et al. 1995)] in fertile men in recent decades—all could have resulted from exposure to endocrine-disrupting chemicals. Recent sperm count studies in the United States do not show such declines, raising the possibility of regional differences in counts, perhaps secondary to differences in environmental exposures (Fisch et al. 1996, Paulsen et al. 1996).

While there are many uncertainties about the causal relationships between endocrine "disrupters" and the observed changes in wildlife and in humans, it seems clear that these compounds have the capacity to compromise the health and survival of a wide variety of species, particularly when these species are exposed to combinations of these compounds, whose synergistic effects may be 1000 times as potent as those from exposures to single compounds (Arnold et al. 1996).

Substances That Alter Immune Functions

A large number of environmental agents can also impair immune system functioning and potentially lead to a loss of species. These include metals like lead, arsenic, and methyl mercury; halogenated aromatic hydrocarbons like PCBs and dioxin; airborne pollutants like nitrogen dioxide, ozone, and sulfur dioxide; solvents like benzene and toluene; and pesticides like chlordane and malathion (National Research Council 1992, Descotes 1988). This is an area of study that has not received the attention it deserves. These immunosuppressant effects could act synergistically with global climate change and ozone depletion to result in significant species morbidity and mortality, affecting humans as well, from infectious diseases and cancers.

Indicator Species

It is a fundamental fact of biology that all living things share a basic chemistry and physiology, and that the closer two organisms are on the evolutionary tree, the more they share. This principle underlies why biomedical laboratory research with animals can be applied, in varying degrees, to human beings. It is also the reason that the study of other species' viability may offer the best window we have for the potential health consequences from environmental degradation for our own species. Some species may be uniquely sensitive to specific environmental changes and thereby be our "canaries" or "indicator species," warning us of potential future harm. In some cases, their vulnerability may be due, not to a greater sensitivity, but to greater exposures, for example, for species at the top of the food chain exposed to unusually high concentrations of toxins through bioaccumulation. Some possible examples deserve mention.

The precipitous drop in common seal (*Phoca vitulina*) populations in the western part (the Dutch area) of the Wadden Sea between 1950 and 1975 (Reijnders 1986), and the reproductive failure among beluga whales (*Delphinapterus leucas*) in the St. Lawrence River in Canada during the 1980s (Beland et al. 1993), offer perhaps models of unusual sensitivity to environmental chemicals that affect fertility. In the case of the seals, ingestion of PCB-contaminated fish, the PCBs most likely coming from the Rhine river, seemed to be the culprit, while for the belugas, there were high tissue concentrations of PCBs, DDT, Mirex (an insecticide that is carried by

eels, a favorite beluga food, migrating from Lake Ontario), lead, and mercury (Martineau et al. 1987). In both cases, these marine mammals, at the top of the marine food chain, concentrated the pollutants involved.

Belugas may also serve as an "indicator species" for immune system dysfunction secondary to pollution, as a high proportion of those studied by scientists at the St. Lawrence National Institute of Ecotoxicology in Canada were diseased, and many died from a variety of tumors and infections (Martineau et al. 1988), presumably because of weakened immune responses (De Guise et al. 1995), resulting from the high levels of known immunotoxins (National Research Council 1992) in their tissues.

With other marine mammals, there is also evidence of possible immunodeficiency states, perhaps caused by their bioaccumulation of toxic chemicals, notably PCBs. Between 1987 and 1992, there have been massive die-offs, involving tens of thousands of seals (Lake Baikal freshwater, common or harbor, grey, monk, ringed, and harp), dolphins (bottlenose, white beaked, and striped), and porpoises (common) in Lake Baikal, the Ionian Sea, the Mediterranean, the North Sea, the Baltic Sea, the Barents Sea, the Gulf of Mexico, and the Atlantic Ocean off the Eastern coast of the United States (Osterhaus et al. 1988, Kennedy et al. 1988, Grachev et al. 1989, Harwood 1989, Domingo et al. 1990, Garrett 1994). These studies have identified four newly discovered viruses of the morbillivirus family (which includes the human measles virus and that causing canine distemper) as the infectious agents responsible. By 1993, the epidemics ended, and although it is still not clear what triggered them [except in the case of Lake Baikal (Grachev et al. 1989)], it has been widely believed that environmental change was the cause. Some researchers have speculated that organochlorine pollution, particularly PCBs, was involved, impairing the immune systems of those animals exposed and resulting in their vulnerability to morbillivirus infections. Many of the carcasses did, in fact, contain high concentrations of these toxins. It was also hypothesized that unusually warm winters led to relatively smaller fish populations and therefore less food for the seals, dolphins, and porpoises, and that the undernourished animals, as a result, mobilized organochlorine immunotoxins into their bloodstreams from stores in body fat. If this were so, then the marine mammal kills might be a case where global climate change and chemical pollution acted synergistically to promote the emergence of a global epidemic.

The hope that mobilliviruses such as those that seemed to decimate marine mammal populations would not infect humans (the only one that was known to do so had been measles) was shattered when 14 racehorses in

Australia died from another new morbillivirus that also infected and killed their trainer (Murray 1995). The underlying cause of this viral outbreak remains a mystery.

Manatees, endangered marine mammals which have lived in waters off the coast of Florida for 45 million years, have also been dying in great numbers. During the first two and one-half months of 1996, some 61 manatees were found dead off southwestern Florida, a number estimated to be almost 10% of the total population in that area (*New York Times* 3/19/96). All of the animals that died had pneumonia, but it is not yet clear what killed the manatees, and what infectious agent or agents caused the pneumonias. The record northward migration of a Florida male manatee to the East River during the summer of 1995, perhaps the result of unusually warm air and ocean temperatures recorded at that time (Sudetic 1995), suggests that increases in ocean temperatures may have had some relationship to the manatee mortality, perhaps secondarily from an increase in toxic red tides from the warming (*New York Times* 4/12/96).

The third example involves amphibians and stratospheric ozone depletion. In recent years, populations of some frogs, toads, and salamanders have declined markedly in many parts of the world, even in pristine habitats far from people (Blaustein and Wake 1990, Wake 1991). Some species may have already become extinct (Blaustein et al. 1994, Blaustein and Wake 1995). These declines have been viewed with alarm by scientists, not only because amphibians are crucial species in some ecosystems, serving as apex predators of invertebrates (including mosquitoes that may carry infectious diseases affecting humans), and as an important food for a wide variety of other species (Pierce 1985) including birds and mammals, but because they have been on the planet for over 100 million years, surviving other great extinctions (such as that of the dinosaurs), so that their current reduced numbers worldwide indicate that global ecosystems may be dangerously unhealthy.

Habitat destruction, particularly in tropical rainforests, is probably the predominant cause of amphibian loss (Blaustein and Wake 1995); other possible causes include acid rain, endocrine-disrupting chemicals (Colborn and Clement 1992), and the introduction of predators and competitors (Blaustein and Wake 1995).

The observation that many of the amphibian species known to be in decline live at high altitudes and lay their eggs in open, often shallow, water led to investigations of the role of UV-B radiation (Blaustein and Wake 1995) in their disappearance. And in 1994, the first conclusive evidence of

UV-B radiation as the likely cause of mortality in some amphibian species was published (Blaustein et al. 1994). The proposed mechanism, that the increased UV-B from stratospheric ozone depletion led to the amphibian eggs' succumbing to opportunistic fungal infections (Blaustein and Wake 1995), raises important questions about possible consequences for other species from thinning of the ozone layer.

The seeming disappearance of Basking sharks—the second largest fish, reaching lengths of 40 feet or more and living for as long as 100 years (*New York Times* 6/27/95)—from many coastal areas around the world may also be an indication of environmental degradation. Some of the loss may be explained by the high prices shark fins command for use in soup [up to $200 a pound (*National Geographic* 1995)] leading to their slaughter, but it is possible that environmental change is also part of the reason. As plankton-eating animals, Basking sharks may be an indicator species for warming of the oceans, which has resulted in significant declines in plankton populations in some regions where Basking sharks have been found in large numbers (Roemmich and McGowan 1995).

Two other examples that demonstrate the unique sensitivity of some species to greenhouse gas emissions and climate change need to be mentioned, as they illustrate the complexity of species responses to changes in the environment, and the potentially serious implications of these changes for ecosystems. The moth (*Helicoverpa armigera*) has recently been shown to be unable to accurately detect small changes in CO_2 released by food plants (as a result of their metabolic activity), because its CO_2 receptor organ is adapted to preindustrial CO_2 concentrations (280 ppm) in the atmosphere and is thrown off by the high concentrations currently present (350 ppm) (Stange and Wong 1993). While this moth is a major agricultural pest and some may rejoice that its destructive habits may be curtailed because of its receptor insensitivity, one must ask if other interactions between insects and plants, some essential for the health of ecosystems or for the viability of food crops such as pollination, are similarly disrupted.

The other example concerns changes in amphibian reproductive cycles in Britain as a consequence of warming temperatures. Several amphibian species of frogs, toads, and newts studied from 1977 to 1994 showed earlier spawning times than usual, the changes closely correlated with the observed increases in average temperatures during the period studied (Beebee 1995). The implications of these changes for the ecosystems in which these amphibians live are not well understood.

Similarly, food crops and livestock may show a marked sensitivity to cli-

mate change, as the highly virulent potato blight during the last several years in the United States, possibly caused by the heavy rains during this time (Dao 1995, Edwards 1996), and the high mortality among cattle and poultry during the July 1995 heat wave across the United States, have demonstrated (*New York Times* 7/14/95). The implications for food production from global climate change, both for agricultural crops and for livestock, is a critically important area that needs much greater attention.

Habitat Destruction

All of the global environmental changes mentioned may contribute to a loss of species and biodiversity, but it is habitat destruction by human activity that is the greatest destroyer. This is especially the case with the destruction of tropical rainforests, which we are cutting or burning at a rate of about 140,000 square kilometers per year, approximately 2% of the amount still standing, an area the size of Switzerland and the Netherlands combined (Wilson 1993).

The diversity of life in these forests is extraordinary. As an example, one investigator found an average of 300 distinct tree species in a series of 1-hectare plots in Peru (Gentry 1988); the total number of native tree species in all of North America is only 700. The same wealth of species diversity has been found for other organisms, and has led many to conclude that tropical rainforests, which comprise only 6% of the world's land mass, contain perhaps 50% of its species. Other species-rich habitats include coral reefs, and the deep oceans.

Only about 1.5 million species have been recorded and given scientific names (May 1988), but new species are being discovered all the time, and it is clear that we have only the barest knowledge of microscopic species like bacteria, fungi, and mites, and of species that have been largely inaccessible, such as in the tropical rain forest canopy, in the deep oceans (Grassle and Maciolek 1992, Hilbig 1994), and even far beneath the Earth's surface (Fredrickson and Onstott 1996). One recent report even described the finding of large numbers of previously undiscovered anaerobic bacterial species at depths of up to 1 mile below the surface of the earth, presumably living there undisturbed since the Triassic epoch (Parkes et al. 1994).

With habitat destruction, we are destroying countless species before we know their identities, and for those that we do know, before we have characterized their chemistries and physiologies.

Implications for Human Health

What are the potential human health consequences of this wholesale destruction?

Loss of Potential Medicines

For one, we are losing plants, animals, and microorganisms that may contain valuable medicines to treat human diseases that are presently untreatable and that cause enormous human suffering. At the present time, a significant proportion of the total pharmaceutical armamentarium is derived from these natural sources. For example, of all the prescriptions dispensed from community pharmacies in the United States from 1959 to 1980, some 25% contained active ingredients extracted from higher plants (Farnsworth 1990), and of the 150 drugs most commonly prescribed in the United States, a significant proportion are derived wholly or in part from natural sources (see Chapter 7). The proportion is even higher in the developing world, where people are more apt to rely on traditional medicines using natural substances.

Many of today's most useful medicines come from tropical rainforests. These include quinine and quinidine from the Cinchona tree (*Cinchona officianalis*), the latter, still one of the most important drugs in treating cardiac arrhythmias; D-tubocurarine, which has revolutionized general surgery by promoting deep muscle relaxation without high doses of general anesthetics, from the Condrodendron vine (*Chondrodendron tomentosum*); streptomycin, neomycin, amphotericin, and erythromycin, widely used antibiotics derived from tropical soil fungi; and vinblastine and vincristine from the Rosy periwinkle plant (*Vinca rosea*), the former extremely effective in treating Hodgkin's disease—achieving marked improvement in 50 to 90% of cases (Calabresi and Chabner 1990)—the latter the most effective agent known against acute childhood leukemias (Calabresi and Chabner 1990).

But it is not only in the tropics that new medicines may be found—temperate regions and the oceans are also vast storehouses of biodiversity, about which extremely little is known. Some examples of drugs from temperate zones include: aspirin, originally extracted from the willow tree (*Salix alba*); digitalis in the forms digoxin and digitoxin, still the main treatment for increasing cardiac contractility in heart failure, from the foxglove plant (*Digitalis purpurea*); and taxol from the Pacific Yew tree (*Taxus brevifolia*). Taxol provides an important example of the potential consequences of

our squandering species in our own backyard, as it was discovered through the National Cancer Institute's screening program for new drugs with anticancer activity in the bark of the Pacific yew, a tree that had originally been discarded during commercial logging in old growth forests of the Pacific Northwest. Original reports showed taxol able to induce remission in 30% of advanced ovarian cancer cases that had been unresponsive to other treatment (McGuire et al. 1989). While some of the initial excitement about taxol as the new cancer wonder drug has waned, it remains an important new advance in cancer chemotherapy and may still be the most promising medication known for the treatment of ovarian and breast cancer (Nicolaou et al. 1996).

Other potential new medicines from temperate organisms that hold great promise include a substance, betulinic acid, from the bark of the white birch, which in laboratory tests has demonstrated marked activity in reducing malignant melanomas (*New York Times* 3/28/95), and salivary anticoagulants from leeches, ticks, blackflies, and other organisms (Bang 1991), which may lead to powerful new anticoagulants.

The oceans, the original home for life on this planet, have barely been explored for new drugs. One on the market, known as cytarabine or ara-C, comes from the Caribbean sponge (*Tethya crypta*), and is one of the most effective agents known for inducing remissions in cases of acute myelocytic leukemia in children and adults (Calabresi and Chabner 1990). Another, bryostatin 1, from the bryozoan *Bugula neritina*, has shown a great deal of promise in Phase 1 trials for inhibiting tumor growth (Prendiville et al. 1993, Philip et al. 1993). Finally, a group of substances called pseudopterosins, extracted from the Caribbean Sea Whip (*Pseudopterogorgia elisbethae*), have been demonstrated to possess anti-inflammatory and analgesic properties more potent than currently available nonsteroidal anti-inflammatory agents such as indomethacin, through mechanisms that have yet to be defined (Look et al. 1986).

Loss of Medical Models

With a loss of species, we are also losing valuable medical models that may help us understand human physiology and disease. Several examples follow.

Dart-poison frogs, the *Dendrobatidae*, from the lowland tropical forests in Central and South America are fast disappearing as they are particularly vulnerable to deforestation (Myers and Daly 1983). Each of the 100 or so species occupies a very specific location in the rainforest and cannot live naturally anywhere else. They are enormously useful to medicine. These

frogs produce some of the deadliest natural toxins known, which have been used for centuries by native Indians to poison arrows and blowgun darts. The active ingredients are alkaloids, and it has been discovered that the reason for their extreme toxicity is that they bind selectively to sodium and potassium channels, calcium pumps, and acetylcholine receptors in nerve and muscle membranes, resulting in paralysis (Albuquerque et al. 1988). One of the toxins, batrachotoxin, for example, binds to a specific site in sodium channels and has been used increasingly by neurophysiologists to understand the structure and function of this most fundamental cellular unit, and to comprehend how nerves and muscles transmit electrical impulses (Albuquerque et al. 1971). If rainforest destruction continues at its present rate, these extremely valuable frogs could be lost.

In many parts of the world bears are also endangered, because of hunting and destruction of their habitats, but in particular, because of the very high prices their body parts bring on the Asian black market for use in traditional medicines and as gourmet food. Bear gallbladders are worth 18 times their weight in gold. The irony is that in medical terms, living bears are worth far more than the sum of all their body parts.

Hibernating, or more accurately denning, bears are biological wonders. Though largely immobile for 4 to 5 months or more, they do not lose bone mass (Floyd et al. 1990). A similar period of immobility or lack of weight bearing results in humans losing one-quarter or more of their bone mass—seen in bedridden and paralyzed patients, in astronauts, and in the inactive elderly. Understanding how bears prevent bone loss during immobility (the only vertebrate that can do this) could lead to ways of preventing or treating osteoporosis, a largely untreatable condition afflicting 25 million Americans, resulting in 1.5 million bone fractures and 50,000 deaths annually (*New York Times* 11/20/94), and costing the U.S. economy $10 billion dollars in direct health care costs and lost productivity each year (National Osteoporosis Foundation 1993).

Bears also do not urinate for the months of denning, as they are somehow able to recycle their urea to make new proteins (Nelson 1987, 1989). Humans, by contrast, unable to excrete their urinary wastes, die after a few days. If we understood how bears accomplished this feat, we might be able to find effective long-term treatments for those with chronic renal failure, who are now totally reliant on dialysis. Renal failure in the United States costs another $7 billion annually, a figure expected to increase to $10 billion by the year 2000 (*New York Times* 11/4/93).

Sharks are also being lost in record numbers from overfishing, and as a result we may never discover why sharks rarely develop tumors or infections, presumably the culmination of 400 million years of successful evo-

lution (Stevens 1992). Some clues have been discovered—MIT researchers have isolated a substance from one shark species, the Basking shark (see page 19), that strongly inhibits the growth of new blood vessels toward solid tissue tumors, thereby preventing their growth (Lee and Langer 1983). This and other work on angiogenesis-inhibiting factors offers one of the best new hopes for developing effective chemotherapeutic agents for some malignant tumors.

Another group of researchers has recently isolated a compound they named squalamine from the tissues of the dogfish shark. Squalamine has demonstrated extremely potent activity in lab tests against a variety of bacteria, fungi, and parasites through mechanisms not yet understood, but that seem entirely different from those of all other known antibiotics (Moore et al. 1993). As infectious agents are developing growing resistance to currently used antibiotics, the search for new drugs working through different pathways becomes increasingly important.

Predatory cone snails of the genus *Conus,* comprising approximately 500 species and found in tropical reef communities, produce a wide variety of toxins to capture their prey. These toxins are small peptides that act on voltage-sensitive calcium channels, sodium channels, *N*-methyl-D-aspartate (NMDA) receptors, nicotinic acetylcholine receptors, and vasopressin receptors in neuromuscular systems (Olivera et al. 1990). They have been increasingly used to understand the molecular structure of these channels and receptors and how they work, to provide clues for the mechanism of action of various human disease conditions, and to find new treatments for these conditions. Calcium channel antagonists derived from *Conus* toxins, for example, have been shown to help alleviate the exaggerated pain responses in some peripheral nerve lesions (Chaplan et al. 1994) and to differentiate the paraneoplastic neuromuscular transmission disorder, Lambert-Eaton syndrome, associated with small-cell lung carcinomas (Lennon et al. 1995) from myasthenia gravis (Miljanich and Ramachandran 1995). The laboratory findings that calcium channel toxins from cone snails also have the potential to prevent neuronal degeneration following focal (Takizawa et al. 1995) and global (Valentino et al. 1993) cerebral ischemia have generated the greatest interest, as these compounds may someday be used to limit nerve cell death in cases of bypass surgery, head trauma, cardiac arrest, and strokes (Miljanich and Ramachandran 1995).

Pit vipers (family *Crotalidae,* which includes rattlesnakes, cobras, and water moccasins) have also become invaluable to medical science. In the 1960s, it was discovered that pit viper venom contained compounds that were lethal to prey because they intensified the animal's response to

bradykinin (Ferreira 1965), a potent vasodilating substance, and thereby caused fatal hypotension. These bradykinin-potentiating factors were shown to be a family of peptides that inhibited kininase II, an enzyme that inactivates bradykinin. Kininase II was subsequently demonstrated to be the same enzyme as angiotensin converting enzyme (ACE), which catalyzes the conversion of angiotensin I, a relatively inactive substance, to angiotensin II, a powerful vasopressor (Garrison and Peach 1990). This understanding of the renin–angiotensin system and of the role of bradykinin gleaned from understanding the action of pit viper venom as an ACE inhibitor led to the development of a whole class of synthetic ACE inhibitors that have become some of the most effective agents known for treating hypertension.

The sea squirt, the only animal besides human beings to form stones naturally in their kidney-like organs, has been used to understand the mechanisms of how kidney stones and gout develop in humans. By studying the formation of both uric acid and calcium oxalate stones in one type of sea squirt, the sea grape (*Molgula manhattensis*), Mary Beth Saffo of the University of California at Santa Cruz is trying to develop strategies for preventing and treating these conditions (Yoon 1994).

The discovery of a new bacterial species, *Thermus aquaticus* (from thermal springs in Yellowstone National Park), which lives at extremely high temperatures (70–75°C) (Brock and Freeze 1969), led to the isolation of polymerase enzymes that have revolutionized DNA and RNA research (Air and Harris 1974) and to countless other applications, including the identification of criminals through their DNA.

Finally, the horseshoe crab (*Limulus polyphemus*), an animal which first evolved 350 million years ago, has proved invaluable in two areas of biomedical research. The first concerns work on vision. Because the horseshoe crab possesses one of the largest and most accessible optic nerves in the animal kingdom, and has the largest photoreceptors of any animal, it has been extensively studied to help understand the fundamental mechanisms of animal vision, and of the way the brain interacts with sensory organs (Hartline et al. 1956, Barlow 1990), insights that may lead to a greater understanding of human vision. The second concerns diagnostic bacteriology. As a result of early discoveries by Frederik Bang on the *Limulus'* clotting response to injections of gram negative bacteria (Bang 1956), the processed blood from the crab, *Limulus* amoebocyte lysate, has developed into one of the most sensitive tests available to detect the presence of gram negative endotoxins. It was because of this test that batches of swine flu vaccine were first shown to be contaminated in the mid 1970s (Sargent 1987).

There are countless other examples of unique microorganisms, plants, and animals holding the secrets of hundreds of millions of years of evolution and hundreds of billions of biological experiments, which, because of species extinctions, are in danger of being lost forever to medical science.

Infectious Diseases

It is important to discuss how alterations in biodiversity can disrupt ecosystem equilibria resulting in the emergence or reemergence of infectious diseases in man. This may be one of the most serious public health consequences of biodiversity loss; it is also perhaps one of the most neglected and poorly understood.

The case of the hantavirus outbreak in the United States serves as a valuable model illustrating the potential effects of such alterations, as well as our relative lack of knowledge about infectious agents in the environment, and the processes that uncover them. Other cases will be discussed more fully in Chapter 2.

Six years of drought in the Four Corners Area of the American Southwest, where Utah, Colorado, Arizona, and New Mexico meet, ended in the late winter and spring of 1993 with unusually heavy snows and rains (Wenzel 1994). These dramatic weather patterns, seen in other parts of the world as well and thought to result directly from an intense and prolonged El Niño (and perhaps indirectly from greenhouse gas-induced warming of the seas), resulted in a superabundance of piñon nuts and grasshoppers, food for the native deer mouse. At the same time, the drought had led to a reduction in the mouse's predators—foxes, snakes, and owls, and as a result, the mouse population exploded, increasing tenfold by May of 1993 over levels of the year before (Wenzel 1994). Deer mice, it was subsequently learned, carry a hantavirus that they shed through their saliva and excreta, and as a consequence of greatly increased exposure by people in the area to the huge mouse population, an epidemic of a rapidly fatal respiratory syndrome developed—17 previously healthy people, most of them Native Americans, initially got the disease; 13 died (Duchin et al. 1994). The number of confirmed cases of hantavirus pulmonary syndrome in the United States has reached 131 in 24 states, mostly in the West, of which almost one-half have been fatal (Freeman 1996).

Other examples of changes in habitats and biodiversity associated with infectious disease spread include Kyasanur Forest Disease, a tickborne hemorrhagic viral disease identified in Mysore, India and linked to deforestation in that region (Morse 1991); Argentine Hemorrhagic Fever, a viral illness carried by a mouse which proliferated and spread with the clearing of the pampas grasslands in Argentina for the purpose of growing corn (Morse 1990); and malaria in the Amazon which has reached epidemic proportions in the past 20 years (Kingman 1989), as a result of forest clearing and the creation of large numbers of still pools where *Anopheles darlingi*, the most important malaria mosquito vector in the area, can multiply unchecked (Walsh et al. 1993). It is not clear whether the recent cases of locally acquired malaria in the United States (Brook et al. 1994, Bell et al. 1995) (which hadn't been seen in 50 years) are also the result of habitat changes, secondary to the unusually warm summers of the past several years which favored the proliferation of native mosquitoes and the transmission of malaria, originally acquired abroad.

These cases illustrate how fragile and complex the equilibria among species in ecosystems are, how little we understand these equilibria, and how a loss of biodiversity (in some cases through changes in weather, but in other cases, perhaps through habitat destruction, the direct elimination of predators, stratospheric ozone depletion, or other means) may result in potentially catastrophic consequences for human beings. No one knows how many viruses or other infectious agents in the environment, potentially harmful to man, are now being held in check by the natural equilibria afforded by biodiversity.

Conclusion

Global climate change, stratospheric ozone depletion, toxic substances released into the environment, and habitat destruction all have the capacity to lead to species extinction and biodiversity loss. Current rates of species loss from human activity rival the great geologic extinctions of the past. With a loss of biodiversity, we risk losing potential new medicines to treat human illnesses that are presently untreatable, foreclosing the possibility of discovering valuable medical models that may help us understand human physiology and disease, and disrupting ecosystem balances on which all life, including human life, depends.

The fundamental relationship between biodiversity and human health is generally unappreciated by policymakers and the public, and as a result, the preservation of habitats and of species is given a low priority. In addition, there is little understanding that the study of species and of biodiversity may offer the best means we have for predicting future dangers to human

beings from environmental degradation, as some species may be affected at lower thresholds to environmental hazards than we are and serve as our "canaries," or so-called "indicator species."

How can the importance of biodiversity become central to the concerns of policymakers and the public? There is a lesson to be learned from the history of chlorofluorocarbons and the ozone layer. Once the magnitude of the danger was clear, and the consequences to human life were obvious, then the world community was able to take effective action to protect the ozone layer. The same must occur with the issue of biodiversity—it is essential that people understand that their health and lives, and those of their children, depend so completely on the health of other species and of global ecosystems. Only then will they develop the motivation to support personal behaviors and public policies that protect biodiversity. There is no task more important for physicians, other health professionals, scientists, and concerned citizens than helping to promote this understanding.

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Global Climate Change and Emerging Infectious Diseases

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Climatic factors influence the emergence and reemergence of infectious diseases, in addition to multiple human, biological, and ecological determinants. Climatologists have identified upward trends in global temperatures and now estimate an unprecedented rise of 2.0°C by the year 2100. Of major concern is that these changes can affect the introduction and dissemination of many serious infectious diseases.

The incidence of mosquito-borne diseases, including malaria, dengue, and viral encephalitides, are among those diseases most sensitive to climate. Climate change would directly affect disease transmission by shifting the vector's geographic range and increasing reproductive and biting rates and by shortening the pathogen incubation period. Climate-related increases in sea surface temperature and sea level can lead to higher incidence of water-borne infectious and toxin-related illnesses, such as cholera and shellfish poisoning. Human migration and damage to health infrastructures from the projected increase in climate variability could indirectly contribute to disease transmission. Human susceptibility to infections might be further compounded by malnutrition due to climate stress on agriculture and potential alterations in the human immune system caused by increased flux of ultraviolet radiation.

Analyzing the role of climate in the emergence of human infectious diseases will require interdisciplinary cooperation among physicians, climatologists, biologists, and social scientists. Increased disease surveillance, integrated modeling, and use of geographically based data systems will afford more anticipatory measures by the medical community. Understanding the linkages between climatological and ecological change as determinants of disease emergence and redistribution will ultimately help optimize preventive strategies.

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EMERGING and reemerging infectious diseases are defined as those increasing in incidence in the recent past or threatening to increase in the near future.[1,2] The entry and subsequent establishment of a pathogen into a new human population must occur for a disease to emerge successfully,[3] and multiple factors with complex interactions are often involved. Climatic conditions play a role in such dynamics, and climatologists have recently identified an accelerated change in long-term global climate trends.[4-10] The assessment of the potential health impacts of these changes now requires evaluation by the medical community.

Many newly emerging diseases in humans are actually long-standing zoonoses of animal host species that surface in human populations after a climatic or environmental change.[2] For example, the pulmonary *Hantavirus* epidemic in the southwest United States was felt to be due to an upsurge in rodent populations related to climate and ecological conditions.[11] Six years of drought, followed by extremely heavy spring rains in 1993, resulted in a 10-fold increase in the population of deer mice, which are the known reservoir of *Hantavirus*.[12,13]

In sub-Saharan Africa, meningococcal meningitis follows a distinct seasonal pattern. Epidemics consistently erupt during the hot dry season and subside soon after the onset of the rainy season.[14] In Nigeria during 1977 through 1979, peak meningitis incidence was strongly correlated with the highest mean maximum temperatures of the season and inversely correlated with absolute humidity to a lesser extent, though still significantly.[15]

In addition to climatological or environmental factors, determinants for emergence include biological, cultural, technological, and socioeconomic factors.[1,3] Changing climate conditions substantially could affect many of these determinants. This article focuses on the more direct effects of climate change on vector and parasite biology and distribution; however, climate's indirect effects on regional food supply and human migration patterns may substantially alter susceptibility to infectious agents.

Assessing how changing climate conditions can alter the life cycles of vectors and parasites is especially critical in understanding the processes behind the emergence or reemergence of many diseases. Diseases in which infectious agents cycle through cold-blooded (invertebrate) species to complete their development are particularly sensitive to subtle climate variations[16,17] compared with diseases spread from human to human. Climate factors strongly determine vector infectivity by affecting pathogen replication, maturation, and the period of infectivity.[18,19] Extreme heat, on the other hand, can shorten insect survival time or disrupt pathogen development.[20]

The geographic range of many vector-borne diseases is limited by climate parameters. For example, the range of the dengue fever vector, the mosquito *Aedes aegypti*, is limited by freezing temperatures that kill overwintering eggs.[21,22] Work by the US National Climatic Data Center demonstrates that minimum temperatures are increasing at a disproportionate rate compared with average and maximum temperatures,[23] and this trend is predicted to continue under climate change scenarios.[5,6] Such conditions may allow parasites and their vector or reservoir hosts to extend into regions previously void of disease.

CLIMATE CHANGE: OBSERVATIONS, PROJECTIONS, AND UNCERTAINTIES

Greenhouse gases (GHGs) allow sunlight to penetrate to the earth's surface, yet prevent infrared radiant heat from escaping. The major anthropogenic GHG is carbon dioxide (CO_2), but methane, nitrous oxide, and chlorofluorocarbons also contribute to radiative climate forcing (warming) by human activity.[10] Fossil fuel emissions and deforestation are the main causes of increasing atmospheric CO_2 (trees sequester carbon and serve as a CO_2 "sink"). Levels of CO_2 have risen by

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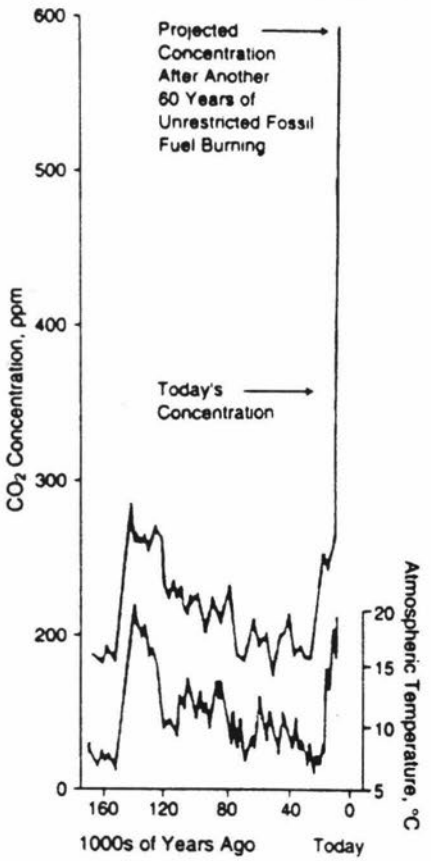


Figure 1.—Global average temperatures (lower line) and carbon dioxide (CO_2) concentration (upper line), 158 000 BC to 1994 AD as determined from Antarctic ice core records (adapted and reprinted with permission from Flavin[26]).

29% (from 278 ppmv to 358 ppmv) since the industrial revolution.[24,25]

Historical records indicate a direct correlation between atmospheric CO_2 levels and average global temperatures[26] (Figure 1). According to the United Nations Intergovernmental Panel on Climate Change, anthropogenic GHG emissions are significantly accelerating current warming trends, which have now been determined to be inconsistent with natural climate variation.[6-8] The global mean surface air temperature has increased approximately 0.5°C over the last 100 years.[5,10] Sea level also has risen by 1 to 2 cm per decade due to climate-related factors, eg, oceanic thermoexpansion and melting of mountain glaciers, as opposed to land subsidence.[27] Mountain snow cover has decreased[6] and oceanographers have recently documented statistically significant deep ocean warming during the period from 1957 through 1992.[28]

The mid-range estimates of future temperature change by the year 2100 are 2.0°C (range, 1.0°C to 3.5°C),[6] or 0.2°C per decade.[9] These figures assume some reduction in the rate of economic growth, plateauing of population rise by the middle of the next century, and an increase in conservation measures. Even if extensive action is immediately taken to reduce GHGs, global temperatures are expected to continue to warm by 0.5°C to 2.0°C by the year 2100.[6,10] Such climate sensitivity to GHG accumulation is consistent with paleontologic data extending over 150 000 years. Mid-value estimates for sea level rise approximate 50 cm by the year 2100.[10,29] This projected rise in both temperature and sea level represents a respective fivefold and threefold faster rate than that observed over the past century.[10,29]

Though model predictions show much agreement, many uncertainties still persist. Major issues include the following: (1) cloud formation from increasing water vapor—depending on altitude, clouds may reflect sunlight (cool) or further insulate (warm); (2) ocean heat capacity—predicting the effect of ocean currents as a buffer to surface warming is still unresolved; (3) sulfate aerosols that cause regional cooling—the most recent climate models now cited by the Intergovernmental Panel on Climate Change are now accounting for these aerosols; (4) CO_2 fertilization of plants—CO_2 enhances photosynthesis in plants increasing their absorption of CO_2, a feedback that potentially could dampen the rise in atmospheric concentrations; (5) the carbon cycle—full accounting for the fate of CO_2 emissions reveals uncertainty in the magnitude of the carbon sink.[10,30] Regarding applications to health, most global climate models do not provide fine enough resolution to predict local conditions that may be pertinent to specific diseases.

While these uncertainties may remain elusive, there is increasing convergence of climate projections arising from independent efforts using diverse methodologies. The medical community is beginning to explore what these predictions might mean for public health. The World Health Organization considers the health ramifications of global warming as one of the largest public health challenges for the upcoming century.[31,32]

VECTOR-BORNE AND WATER-BORNE DISEASES

Changing trends in average temperature and precipitation are anticipated to have an impact on vector-borne disease incidence and distribution. Diseases expected to be affected by climate change are listed in Table 1 from the World Health Organization.[31] The following sections will illustrate how some of the major mosquito-borne diseases may extend or intensify with climate change. They include (1) malaria; (2) dengue and dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS); and (3) arboviral encephalitides. Water-borne diseases associated with temperature-sensitive marine ecosystems will also be addressed, and include (4) cholera, found to be harbored by zooplankton; and (5) toxic, rather than infectious, algae (red tides).

Direct Effects on Specific Reemerging Diseases

Malaria.—Malaria is the most prevalent vector-borne disease globally and causes 1 million to 2 million deaths annually.[33] A marked resurgence of malaria has occurred since 1973,[34] and according to the Institute of Medicine, efforts to control malaria have been disappointing. More than 50 mosquito species have developed resistance to insecticides since 1947.[35] Drug resistance persists for the most virulent species, *Plasmodium falciparum*, and antimalarial vaccines have shown only limited efficacy.[33,36,37] In many regions where malaria transmission had been almost eliminated, the disease has made a comeback, sometimes surpassing earlier recorded levels.[33]

Malaria generally extends to the 16°C winter isotherm, since parasite development does not occur below this temperature.[34,38] Temperature and humidity are among the most important factors for disease transmission and the extrinsic incubation period (EIP) of the parasite shortens dramatically at temperatures between 20°C and 27°C.[30,34] The EIP is defined as the number of days between the vector's ingestion of an infected blood meal and the point that it becomes capable of transmitting infection. Climatic factors that increase the inoculation rate of *Plasmodium* pathogens, as well as the breeding activity of *Anopheles* mosquitoes, are considered the most important cause of epidemic outbreaks of malaria in nonendemic areas.[34]

Malaria incidence related to local climatic change has been observed in Rwanda, when in 1987, extension of malaria into higher altitudes resulted after record high temperatures and rainfall.[39] Monthly malaria incidence in high-altitude regions was exponentially affected by changes in minimum temperature. In low-altitude zones, rainfall and mean temperature were the most significant climatic factors. In Zimbabwe, temperature defines malaria distribution as well, since malaria incidence and prevalence are strongly linked to altitude (Figure 2).[40]

Based on such observations, a relatively small increase in winter (minimum) temperature would likely facilitate the spread of malaria into large urban highland populations that are currently malaria-free and immunologically naive, such as Nairobi, Kenya, and Harare, Zimbabwe. According to malaria models under climate

Status of Major Vector-borne Diseases and Predicted Sensitivity to Climate Change*

Disease	Populations at Risk, Millions†	Prevalence of Infection, Millions‡	Present Distribution	Possible Change of Distribution as a Result of Climatic Change
Malaria	2100	270	Tropics, subtropics	Highly likely
Lymphatic filariases	900	90 2	Tropics, subtropics	Likely
Onchocerciasis	90	17 8	Africa, Latin America	Likely
Schistosomiasis	600	200	Tropics, subtropics	Very likely
African trypanosomiasis	50	25 000 new cases per year	Tropical Africa	Likely
Leishmaniasis	350	12 million infected + 400 000 new cases per year	Asia, southern Europe, Africa, South America	Not known
Dracunculiasis	63	1	Tropics (Africa, Asia)	Unlikely
Arboviral diseases				
Dengue			Tropics, subtropics	Very likely
Yellow fever			Africa, Latin America	Likely
Japanese encephalitis			East and Southeast Asia	Likely
Other arboviral diseases	...	...	Tropical to temperate zones	Likely

*Data from World Health Organization.[31]
†Based on a world population estimated at 4.8 billion (1989).
‡Ellipses indicate no estimates available.

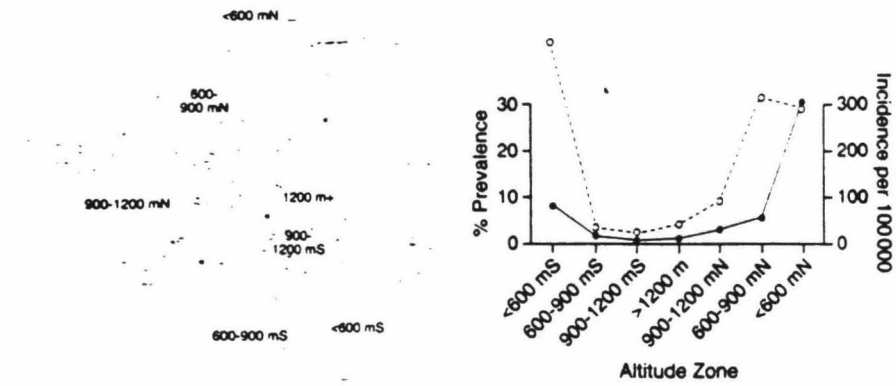


Figure 2.—Left, altitude classification of Zimbabwe and, right, average annual malaria prevalence (solid line) and incidence (dotted line) per 100 000 population by altitude zone; mS indicates meters, South; m, meters; mN, meters, North; and m+, 1200 meters and higher. Prevalence data are from 1969 through 1981 and incidence data are from 1972 through 1981 (adapted and reprinted with permission from Taylor and Mutambu[49]).

change scenarios,[41,42] risk of malaria epidemics would rise substantially in both tropical and temperate regions. An estimated 1 million additional fatalities per year could be attributed to climate change by the middle of the next century, according to one model.[43]

Dengue and Dengue Hemorrhagic Fever/Dengue Shock Syndrome.—Globally, 520 arthropod-borne viruses, or arboviruses, have been identified, of which over 100 can produce human disease.[2,44] Dengue and yellow fever are due to flaviviruses and share the same principal mosquito vector, *Ae aegypti*. Urbanization, inadequate mosquito control, absence of water systems, and international travel or migration are major factors leading to the reemergence of dengue.[45,46] Climate conditions, however, contribute to epidemic spread and geographic distribution.[47,48]

Dengue, or "breakbone fever," is a severe viral illness occurring sporadically and in epidemics.[49] Unlike yellow fever, there is no vaccine or antiviral pharmaceutical available for dengue. Outbreaks in urban areas infested with *Ae aegypti* may be explosive, with up to 70% to 80% of the populations involved.[50] In the 1950s, the more severe DHF/DSS appeared in Southeast Asia, and is thought to be caused by sequential infection by any two of the four serotypes of the dengue virus in hyperendemic locations.[51] Between 250 000 and 500 000 DHF/DSS cases occur yearly throughout the world, and case fatality rates approach 40% to 50% if untreated,[44] and 1% to 5% with appropriate fluid replacement therapy.[52] Since the late 1970s dengue has reemerged and DHF/DSS has emerged in the Americas.[45,46,50]

Currently, dengue viruses are being transmitted in the tropics between 30° north and 20° south latitude,[53] since frosts or sustained cold weather kills adult mosquitoes and overwintering eggs and larvae.[22,54] Warming trends, therefore, can shift vector and disease distribution to higher latitudes or altitudes, as was observed in Mexico when dengue reached an altitude of 1700 m during an unseasonably warm summer in 1988.[55] Other epidemiological studies help confirm this relationship between dengue and temperature. During the 1978-1979 epidemic in Honduras, no endemic dengue occurred in Tegucigalpa, where average temperatures are 4°C cooler than the coastal lowlands.[56] In Mexico in 1986, the most important predictor of dengue prevalence was found to be the median temperature during the rainy season, with an adjusted fourfold increase observed between 17°C and 30°C.[57]

Temperature also affects the transmission dynamics of dengue. Warmer temperatures reduce larval size of *Ae aegypti*, ultimately affecting adult size.[58] Smaller adults must feed more frequently to develop an egg batch,[47,59] boosting the incidence of double feeding within each gonotrophic cycle.[47] This direct relationship between biting rates and temperature has been found in field studies from Thailand.[60] Regarding viral development, the EIP shortens with higher temperatures,[48,61] increasing the proportion of mosquitoes that become infectious at a given time.[62] For example, the EIP for dengue type-2 virus requires 12 days at 30°C and only 7 days at 32°C to 35°C.[61] Shortening the incubation period by 5 days translates to a potential threefold higher transmission rate of disease.[57] In short, slightly higher temperatures within the range of mosquito viability lead to more infectious mosquitoes that bite more frequently.

Arboviral Encephalitis.—Of reported encephalitis cases in the United States, 65% are of arboviral etiology.[63] Most are mosquito-borne and, in order of prevalence in the United States, include the following: St Louis encephalitis (SLE) and La Crosse encephalitis, and western, eastern, and Venezuelan equine encephalomyelitis. Clinical features of the most common North American pathogenic arbovirus, SLE, range from headache to aseptic meningitis and encephalitis, with the elderly at highest risk for mortality. Epidemics generally occur south of the 20°C June isotherm, but northerly outbreaks have occurred during unseasonably warm years.[63]

Several vector species exist for SLE: *Culex tarsalis* in the rural west where SLE is endemic, *Culex nigripalpus* in Florida, *Culex pipiens quinquefasciatus* in the urban southeast, and *Culex pipiens pipiens* in the urban north.[63] Human outbreaks of SLE are highly correlated with several-day periods when temperature exceeds 30°C (85°F),[64] as was the case during the 1984 California epidemic that followed a period of extremely

high temperatures. Precipitation patterns are also important for transmission.[66] Computer analysis of monthly climate data has demonstrated that excessive rainfall in January and February, in combination with drought in July, most often precedes SLE outbreaks.[66] Such a pattern of warm, wet winters followed by hot, dry summers closely resembles the computer global circulation model projections for climate change in the United States.[4,5,67]

From field studies in California, a 1°C increase in temperature corresponds to a 1% decrease in adult mosquito mean daily survivorship.[68] Offsetting this potential benefit, viral transmission rates rise sharply at higher temperatures (Figure 3).[69,70] From their results, Reeves et al, predict that a 3°C to 5°C temperature increase will cause a significant northern shift in both western equine encephalitis and SLE outbreaks, with disappearance of western equine encephalitis in southern endemic regions.

Other Vector-borne Diseases.—Schistosomiasis has increased in prevalence in arid warm regions primarily from expansion of irrigation systems where snails serve as the intermediate host. Water shortages predicted for many agricultural areas could thus potentiate further risk in these regions by increasing demand for irrigation. Also, warmer temperature influences infectivity and development of the parasite within the snail. During winter, cercarial infection in water snails becomes dormant and potential transmission sharply diminishes.[71,72] Therefore, if temperatures increase, snails could spread schistosomiasis over a longer period during the year.[31,73] Recent modeling of schistosomiasis predicts an additional 5 million cases attributed to climate change by the year 2050.[74]

Onchocerciasis, or "river blindness," is a blackfly-borne disease primarily found in West Africa and, to a lesser extent, in Latin America. Climate plays an important role in the occurrence of onchocerciasis since the vector requires fast-flowing water for successful reproduction, and the adult vector can be spread by wind.[75] A recent study found that if temperature and precipitation change across portions of West Africa as predicted by some global circulation models, blackfly populations may increase by as much as 25% at their current breeding sites.[76] Potential abandonment of agricultural land in river valleys could add to regional food production problems.

African trypanosomiasis, or "sleeping sickness," is carried by tsetse flies, whose distribution depends on vegetation cover. Researchers in sub-Saharan Africa have correlated vegetation type to the population densities of tsetse flies using satellite images to predict a large extension of regions at risk for this disease, assuming a 3°C mean monthly temperature rise.[77,78]

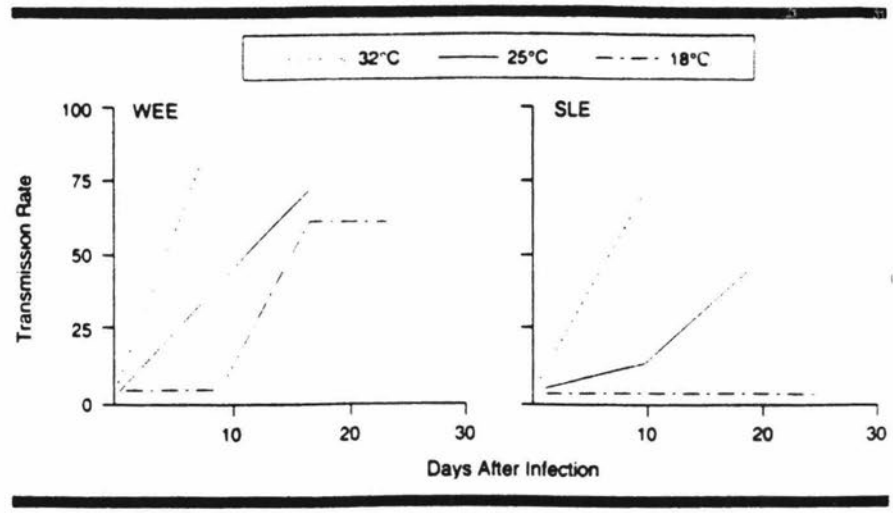


Figure 3.—Effect of temperature on transmission rates (the percentage of bites that result in transmission) of Western equine encephalitis (WEE) and St Louis encephalitis (SLE) viruses by the mosquito, *Culex tarsalis* (reprinted with permission from Reeves et al[68]).

Tick-borne diseases are also sensitive to climatic conditions but favor cooler temperatures. In Africa, Rogers and Randolph found mean monthly maximum temperature to be the strongest predictor of tick occurrence at the margins of endemic zones.[79] Only 2°C determined the difference between areas where ticks are present or absent in southeastern Africa. In the southern United States, Rocky Mountain spotted fever may decline due to ticks' intolerance of high temperatures and diminished humidity.[80]

Cholera and Toxic Algae

During the past decade, phytoplanktologists have reported an unusual spread and intensity of algal blooms worldwide.[81] Increases in phytoplankton (or algae) globally have been a consequence of wetland loss, poor erosion control management, liberal agricultural application of fertilizers, and coastal sewage release, all resulting in effluents rich in nutrients that promote algae growth. These growth-favoring factors could be augmented by warmer sea surface temperatures expected with global climate change.

Over the past century, average sea surface temperature has increased approximately 0.7°C,[5] and marine growth of algae has been observed to respond to localized temperature increases in nutrient-replete waters. For example, one species of toxic phytoplankton previously confined to the Gulf of Mexico, *Gymnodinium breve*, extended northward in 1987 after a "parcel of warm gulf stream water" reached far up the East Coast resulting in human neurological shellfish poisonings and substantial fishkills.[82] Red tides, which cause paralytic shellfish poisoning, diarrheic shellfish poisoning, and amnesiac shellfish poisoning are blooms of toxic dinoflagellates. Warm water favors the growth of dinoflagellates and cyanobacteria that include more toxic organisms.[83]

Zooplankton, which feed on algae, can serve as reservoirs for *Vibrio cholerae* and other enteric pathogens, particularly gram-negative rods.[84] Large coastal blooms may have contributed to the recent multi-epicentered cholera pandemic in Latin America. Using fluorescent antibody techniques, forms of quiescent *V cholerae* have been found to persist on the sheaths and exoskeletons of marine organisms that can revert to a culturable state when nutrients, pH, and temperature permit.[85]

In October 1991, algal paralytic saxotoxins were detected for the first time in Chilean waters as far south as the Straits of Magellan.[86] The unusual and prolonged extension into new areas led to approximately 300 cases of intoxication from shellfish, including 11 deaths. This southern extension, coinciding with the penetration of cholera into Latin America, lends credence to the hypothesis that coastal algal blooms were associated with the intensity and breadth of the current pandemic. Climatologists are beginning to question whether large-scale changes in marine ecosystems are already indicative of sea-surface warming due to the greenhouse effect.[87]

Extreme Weather Events and Climate Variability

In addition to sea level rise, more frequent extreme weather events are predicted to accompany global warming.[7,88] Severe storms can cause contamination of water systems and simultaneously create breeding sites for insects or favorable conditions for rodents that carry diseases. Destruction of shelters leaves human

populations more exposed to infectious vectors, increasing the potential for epidemics.

Human migration away from coastal, rural, or other economically or physically vulnerable locations could be anticipated. Many regions throughout the tropics and subtropics have been identified as being vulnerable to an increase in extreme weather events.[89] The potential risk of epidemics could increase in urban settings as refugees arrive from disease-endemic areas.[90,91] Already, current trends in urbanization increase the potential for disease epidemics such as cholera and dengue fever.

El Niño.—Some of the anticipated health impacts associated with extreme climate variability are already within the range of current human experience. Many disease outbreaks have been associated with the erratic weather conditions driven by El Niño Southern Oscillation (ENSO) events. ENSO is a climate phenomenon that is second only to seasonal cycles in its impacts on regional climate variability,[92] and occur on average every 4 years.[93] Anomalous fluctuations in precipitation, even to the extent of floods or droughts, are known to result from climate variations influenced by ENSO events.

Extreme heavy rainfalls have been correlated with outbreaks of Murray Valley encephalitis and Ross River virus in Australia, eastern equine encephalitis in the United States,[92] West Nile fever in southern Africa,[94] and cyclical malaria epidemics in Argentina[95] and Pakistan.[96] Such climate-related outbreaks have closely corresponded to ENSO cycles, which are now thought to be the driving force behind these geographically specific extreme climatic conditions.[97,98] Malaria can also be associated with droughts linked to ENSO phenomenon that create pools from rivers in Sri Lanka.[97] The agriculturally devastating drought in countries of the Indian Ocean region in the past several years has been attributed to a persistent El Niño, as well.[94]

These ENSO-related outcomes may serve as an analogue for analyzing repercussions from long-term changes in climate variability and extremes. Furthermore, some evidence suggests that ENSO events may become more frequent as the earth warms,[99,100] and variability in the incidence of vector-borne diseases will likely increase as a result of global greenhouse warming.[92]

INDIRECT EFFECTS ON HUMAN SUSCEPTIBILITY

Agriculture and Human Nutrition

Climate change could adversely affect agriculture both by long-term changes, such as reducing soil moisture through evapotranspiration, and more immediately, by extreme weather events such as droughts, flooding (and erosion), and tropical storms.[101] Sea level rise could affect food production through the combination of inundation and increased salinity of coastal farmlands.

On the other hand, "CO_2 fertilization" enhances photosynthesis and may initially benefit plants.[102] Accounting for this beneficial effect, a study involving 30 nations still estimated that 40 million to 300 million additional people worldwide could be at risk from hunger due to climate change.[103] This study adjusted for predicted international trade liberalization that would be expected to ameliorate regional food shortages. The potentially large impact of changing distribution of plant pests and pathogens is a relative unknown.

Ultraviolet-Induced Immunosuppression: Potential for Synergism?

Stratospheric ozone depletion, accompanied by increases in ambient, biologically destructive ultraviolet-B radiation,[104] may exacerbate the effect of climate change on infectious diseases. Arising from a different anthropogenic process than climate change, ozone destruction is occurring primarily from reactions between ozone and halogen free radicals derived from chlorofluorocarbons, other halocarbons, and methyl bromide.[105] In addition to causing skin cancer and cataracts,[106,107] ultraviolet light has been shown to cause immunosuppression in both animal and human studies.[106,108-114] Ultraviolet-B radiation impairs antigen processing and presentation by Langerhan cells at the local level,[115-117] as well as altering lymphokine production, which reduces T-helper and T-suppressor cell ratios at the systemic level.[118-122]

Exposure can affect the course of infectious diseases of the skin such as onchocerciasis and dermatophytosis, and diseases where the skin is a portal of entry, as in leishmaniasis.[123] A recent human study found ultraviolet radiation to impair granulomatous delayed-type hypersensitivity response to leprosy antigens, suggesting the potential for ultraviolet-related impaired defense against intracellular pathogens.[109] In short, increased ultraviolet-B exposure may augment the potential for disease emergence and dissemination by lowering human immune defenses.

CONCLUSION AND RECOMMENDATIONS

To facilitate primary prevention of emerging infectious diseases, greater predictive capability needs to be developed. This will require new, interdisciplinary methods of analysis and response strategies. Unlike classical epidemiological focus on attack rates and human populations, understanding emerging infectious diseases will require a broader focus on ecosystem dynamics, including climate variables, habitat characteristics, and host and vector species populations, aside from human disease parameters.[124-126] Mathematical models have recently been developed that integrate many of these variables in an attempt to predict disease incidence.[41,42,74,127]

An essential step in recognizing and thereby mitigating the emergence of infectious diseases is enhanced surveillance and response. Attention needs to be directed toward establishing sentinel diagnostic centers in sensitive geographic regions bordering endemic zones.[89] Such detection will not only provide an early warning for possibly more pervasive changes in disease behavior and allow for intervention, but will also enrich our knowledge of climate-related diseases and facilitate the creation of better predictive models.

In September 1995, the US National Academy of Sciences, the Institute of Medicine, and the National Science and Technology Council cosponsored an international conference on "Human Health and Global Climate Change." Currently, the National Academy of Sciences and the Institute of Medicine are jointly considering undertaking a comprehensive interdisciplinary study of the relationship between climate and infectious diseases.

The diseases mentioned in this article help illustrate the linkages between climate, ecosystems, and human health. Better understanding of these relationships will require new analytical tools and cooperation between physicians on the one hand, and climatologists, biologists, and social scientists on the other.[128] Examples of useful analytical tools include geographic information systems to organize geographically based disease, climate, and demographic data, and remote satellite sensing technology that provides valuable data on land use patterns, habitat characteristics, and marine ecosystems.[129] In recent studies, geographic information systems and satellite-generated vegetative index maps were used to identify areas receptive to dengue fever and Lyme disease in the United States, schistosomiasis in Egypt and the Philippines, and malaria in temperate rice-growing regions.[129,130]

Disease emergence and reemergence have multiple determinants. Climate variables can influence disease processes at varying levels, from directly affecting pathogen maturation and vector reproduction, to altering vector or host habitats, human nutrition, and human demographics. Global climate change can alter the distribution of infectious diseases,

placing new and potentially large human populations at risk. Many of the impacts of climate change may become evident only over an extended period, given the inertia of the climate system. Alternatively, some of the recent examples of emerging infectious diseases may already reflect early changes in long-term trends of climatic means and/or variability. In either case, the potential impacts of climate change on the sustainability of public health combined with the difficulty of reversing ecosystem changes once they have occurred, warrant increased efforts by the medical community in addressing this problem in a concerted and timely fashion.

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Look to Weather for Clues to Malaria Comeback

To the Editor:

"Malaria Makes a Comeback, and Is More Deadly Than Ever" (front page, Jan. 8) captures the multiple factors — population movements, chemical resistance, lapsed public health vigilance and environmental change — influencing the resurgence of malaria. Mosquitoes, the transmitters of the disease, are indeed quintessential opportunists and adapt readily in disturbed environments.

As co-author of the World Health Organization report discussed in your article, I offer several recent findings. Consistent with model projections that global warming could hasten the geographic spread of malaria and dengue fever, these devastating diseases are now occurring at high altitudes in Latin America, central Africa and Asia. Cerebral malaria has occurred in Nairobi, Kenya, while dengue fever is found in the mountains around San José, Costa Rica.

Moreover, highland malaria and dengue fever are occurring in the context of upward migration of plants on many continents and summit glacial retreat in Latin America, Europe, central Africa and Asia. A recent study in the journal Nature confirmed that the freezing levels in the mountains have indeed shifted upward about 500 feet since 1970, representing a warming of close to 2 degrees Fahrenheit.

As we enter a year of debate concerning climate change (the convention will be held in Kyoto, Japan, in December), it is prudent to examine the potential consequences associated with continued warming and climate instability. Your article says that malaria "hinders economic development"; epidemics are growing ever more costly in terms of health, development, trade and tourism.



Lars Leetaru

While the resurgence of infectious disease has multiple social, biological and environmental roots, meteorological factors may play an increasing role in the future. We may be vastly underestimating the social and economic damages associated with epidemics and extreme weather events as well as the potential benefits to society as a whole of changing our environmental and energy policies.

PAUL R. EPSTEIN, M.D.
Boston, Jan. 8, 1997

The writer is associate director of the Center for Health and the Global Environment at Harvard Medical School.

Substances That Alter Immune Functions

A large number of environmental agents can also impair immune system functioning and potentially lead to a loss of species. These include metals like lead, arsenic, and methyl mercury; halogenated aromatic hydrocarbons like PCBs and dioxin; airborne pollutants like nitrogen dioxide, ozone, and sulfur dioxide; solvents like benzene and toluene; and pesticides like chlordane and malathion (National Research Council 1992, Descotes 1988). This is an area of study that has not received the attention it deserves. These immunosuppressant effects could act synergistically with global climate change and ozone depletion to result in significant species morbidity and mortality, affecting humans as well, from infectious diseases and cancers.

Indicator Species

It is a fundamental fact of biology that all living things share a basic chemistry and physiology, and that the closer two organisms are on the evolutionary tree, the more they share. This principle underlies why biomedical laboratory research with animals can be applied, in varying degrees, to human beings. It is also the reason that the study of other species' viability may offer the best window we have for the potential health consequences from environmental degradation for our own species. Some species may be uniquely sensitive to specific environmental changes and thereby be our "canaries" or "indicator species," warning us of potential future harm. In some cases, their vulnerability may be due, not to a greater sensitivity, but to greater exposures, for example, for species at the top of the food chain exposed to unusually high concentrations of toxins through bioaccumulation. Some possible examples deserve mention.

The precipitous drop in common seal (*Phoca vitulina*) populations in the western part (the Dutch area) of the Wadden Sea between 1950 and 1975 (Reijnders 1986), and the reproductive failure among beluga whales (*Delphinapterus leucas*) in the St. Lawrence River in Canada during the 1980s (Beland et al. 1993), offer perhaps models of unusual sensitivity to environmental chemicals that affect fertility. In the case of the seals, ingestion of PCB-contaminated fish, the PCBs most likely coming from the Rhine river, seemed to be the culprit, while for the belugas, there were high tissue concentrations of PCBs, DDT, Mirex (an insecticide that is carried by

eels, a favorite beluga food, migrating from Lake Ontario), lead, and mercury (Martineau et al. 1987). In both cases, these marine mammals, at the top of the marine food chain, concentrated the pollutants involved.

Belugas may also serve as an "indicator species" for immune system dysfunction secondary to pollution, as a high proportion of those studied by scientists at the St. Lawrence National Institute of Ecotoxicology in Canada were diseased, and many died from a variety of tumors and infections (Martineau et al. 1988), presumably because of weakened immune responses (De Guise et al. 1995), resulting from the high levels of known immunotoxins (National Research Council 1992) in their tissues.

With other marine mammals, there is also evidence of possible immunodeficiency states, perhaps caused by their bioaccumulation of toxic chemicals, notably PCBs. Between 1987 and 1992, there have been massive die-offs, involving tens of thousands of seals (Lake Baikal freshwater, common or harbor, grey, monk, ringed, and harp), dolphins (bottlenose, white beaked, and striped), and porpoises (common) in Lake Baikal, the Ionian Sea, the Mediterranean, the North Sea, the Baltic Sea, the Barents Sea, the Gulf of Mexico, and the Atlantic Ocean off the Eastern coast of the United States (Osterhaus et al. 1988, Kennedy et al. 1988, Grachev et al. 1989, Harwood 1989, Domingo et al. 1990, Garrett 1994). These studies have identified four newly discovered viruses of the morbillivirus family (which includes the human measles virus and that causing canine distemper) as the infectious agents responsible. By 1993, the epidemics ended, and although it is still not clear what triggered them [except in the case of Lake Baikal (Grachev et al. 1989)], it has been widely believed that environmental change was the cause. Some researchers have speculated that organochlorine pollution, particularly PCBs, was involved, impairing the immune systems of those animals exposed and resulting in their vulnerability to morbillivirus infections. Many of the carcasses did, in fact, contain high concentrations of these toxins. It was also hypothesized that unusually warm winters led to relatively smaller fish populations and therefore less food for the seals, dolphins, and porpoises, and that the undernourished animals, as a result, mobilized organochlorine immunotoxins into their bloodstreams from stores in body fat. If this were so, then the marine mammal kills might be a case where global climate change and chemical pollution acted synergistically to promote the emergence of a global epidemic.

The hope that mobilliviruses such as those that seemed to decimate marine mammal populations would not infect humans (the only one that was known to do so had been measles) was shattered when 14 racehorses in

Australia died from another new morbillivirus that also infected and killed their trainer (Murray 1995). The underlying cause of this viral outbreak remains a mystery.

Manatees, endangered marine mammals which have lived in waters off the coast of Florida for 45 million years, have also been dying in great numbers. During the first two and one-half months of 1996, some 61 manatees were found dead off southwestern Florida, a number estimated to be almost 10% of the total population in that area (*New York Times* 3/19/96). All of the animals that died had pneumonia, but it is not yet clear what killed the manatees, and what infectious agent or agents caused the pneumonias. The record northward migration of a Florida male manatee to the East River during the summer of 1995, perhaps the result of unusually warm air and ocean temperatures recorded at that time (Sudetic 1995), suggests that increases in ocean temperatures may have had some relationship to the manatee mortality, perhaps secondarily from an increase in toxic red tides from the warming (*New York Times* 4/12/96).

The third example involves amphibians and stratospheric ozone depletion. In recent years, populations of some frogs, toads, and salamanders have declined markedly in many parts of the world, even in pristine habitats far from people (Blaustein and Wake 1990, Wake 1991). Some species may have already become extinct (Blaustein et al. 1994, Blaustein and Wake 1995). These declines have been viewed with alarm by scientists, not only because amphibians are crucial species in some ecosystems, serving as apex predators of invertebrates (including mosquitoes that may carry infectious diseases affecting humans), and as an important food for a wide variety of other species (Pierce 1985) including birds and mammals, but because they have been on the planet for over 100 million years, surviving other great extinctions (such as that of the dinosaurs), so that their current reduced numbers worldwide indicate that global ecosystems may be dangerously unhealthy.

Habitat destruction, particularly in tropical rainforests, is probably the predominant cause of amphibian loss (Blaustein and Wake 1995); other possible causes include acid rain, endocrine-disrupting chemicals (Colborn and Clement 1992), and the introduction of predators and competitors (Blaustein and Wake 1995).

The observation that many of the amphibian species known to be in decline live at high altitudes and lay their eggs in open, often shallow, water led to investigations of the role of UV-B radiation (Blaustein and Wake 1995) in their disappearance. And in 1994, the first conclusive evidence of

UV-B radiation as the likely cause of mortality in some amphibian species was published (Blaustein et al. 1994). The proposed mechanism, that the increased UV-B from stratospheric ozone depletion led to the amphibian eggs' succumbing to opportunistic fungal infections (Blaustein and Wake 1995), raises important questions about possible consequences for other species from thinning of the ozone layer.

The seeming disappearance of Basking sharks—the second largest fish, reaching lengths of 40 feet or more and living for as long as 100 years (*New York Times* 6/27/95)—from many coastal areas around the world may also be an indication of environmental degradation. Some of the loss may be explained by the high prices shark fins command for use in soup [up to $200 a pound (*National Geographic* 1995)] leading to their slaughter, but it is possible that environmental change is also part of the reason. As plankton-eating animals, Basking sharks may be an indicator species for warming of the oceans, which has resulted in significant declines in plankton populations in some regions where Basking sharks have been found in large numbers (Roemmich and McGowan 1995).

Two other examples that demonstrate the unique sensitivity of some species to greenhouse gas emissions and climate change need to be mentioned, as they illustrate the complexity of species responses to changes in the environment, and the potentially serious implications of these changes for ecosystems. The moth (*Helicoverpa armigera*) has recently been shown to be unable to accurately detect small changes in CO_2 released by food plants (as a result of their metabolic activity), because its CO_2 receptor organ is adapted to preindustrial CO_2 concentrations (280 ppm) in the atmosphere and is thrown off by the high concentrations currently present (350 ppm) (Stange and Wong 1993). While this moth is a major agricultural pest and some may rejoice that its destructive habits may be curtailed because of its receptor insensitivity, one must ask if other interactions between insects and plants, some essential for the health of ecosystems or for the viability of food crops such as pollination, are similarly disrupted.

The other example concerns changes in amphibian reproductive cycles in Britain as a consequence of warming temperatures. Several amphibian species of frogs, toads, and newts studied from 1977 to 1994 showed earlier spawning times than usual, the changes closely correlated with the observed increases in average temperatures during the period studied (Beebee 1995). The implications of these changes for the ecosystems in which these amphibians live are not well understood.

Similarly, food crops and livestock may show a marked sensitivity to cli-

mate change, as the highly virulent potato blight during the last several years in the United States, possibly caused by the heavy rains during this time (Dao 1995, Edwards 1996), and the high mortality among cattle and poultry during the July 1995 heat wave across the United States, have demonstrated (*New York Times* 7/14/95). The implications for food production from global climate change, both for agricultural crops and for livestock, is a critically important area that needs much greater attention.

Habitat Destruction

All of the global environmental changes mentioned may contribute to a loss of species and biodiversity, but it is habitat destruction by human activity that is the greatest destroyer. This is especially the case with the destruction of tropical rainforests, which we are cutting or burning at a rate of about 140,000 square kilometers per year, approximately 2% of the amount still standing, an area the size of Switzerland and the Netherlands combined (Wilson 1993).

The diversity of life in these forests is extraordinary. As an example, one investigator found an average of 300 distinct tree species in a series of 1-hectare plots in Peru (Gentry 1988); the total number of native tree species in all of North America is only 700. The same wealth of species diversity has been found for other organisms, and has led many to conclude that tropical rainforests, which comprise only 6% of the world's land mass, contain perhaps 50% of its species. Other species-rich habitats include coral reefs, and the deep oceans.

Only about 1.5 million species have been recorded and given scientific names (May 1988), but new species are being discovered all the time, and it is clear that we have only the barest knowledge of microscopic species like bacteria, fungi, and mites, and of species that have been largely inaccessible, such as in the tropical rain forest canopy, in the deep oceans (Grassle and Maciolek 1992, Hilbig 1994), and even far beneath the Earth's surface (Fredrickson and Onstott 1996). One recent report even described the finding of large numbers of previously undiscovered anaerobic bacterial species at depths of up to 1 mile below the surface of the earth, presumably living there undisturbed since the Triassic epoch (Parkes et al. 1994).

With habitat destruction, we are destroying countless species before we know their identities, and for those that we do know, before we have characterized their chemistries and physiologies.

Implications for Human Health

What are the potential human health consequences of this wholesale destruction?

Loss of Potential Medicines

For one, we are losing plants, animals, and microorganisms that may contain valuable medicines to treat human diseases that are presently untreatable and that cause enormous human suffering. At the present time, a significant proportion of the total pharmaceutical armamentarium is derived from these natural sources. For example, of all the prescriptions dispensed from community pharmacies in the United States from 1959 to 1980, some 25% contained active ingredients extracted from higher plants (Farnsworth 1990), and of the 150 drugs most commonly prescribed in the United States, a significant proportion are derived wholly or in part from natural sources (see Chapter 7). The proportion is even higher in the developing world, where people are more apt to rely on traditional medicines using natural substances.

Many of today's most useful medicines come from tropical rainforests. These include quinine and quinidine from the Cinchona tree (*Cinchona officianalis*), the latter, still one of the most important drugs in treating cardiac arrhythmias; D-tubocurarine, which has revolutionized general surgery by promoting deep muscle relaxation without high doses of general anesthetics, from the Condrodendron vine (*Chondrodendron tomentosum*); streptomycin, neomycin, amphotericin, and erythromycin, widely used antibiotics derived from tropical soil fungi; and vinblastine and vincristine from the Rosy periwinkle plant (*Vinca rosea*), the former extremely effective in treating Hodgkin's disease—achieving marked improvement in 50 to 90% of cases (Calabresi and Chabner 1990)—the latter the most effective agent known against acute childhood leukemias (Calabresi and Chabner 1990).

But it is not only in the tropics that new medicines may be found—temperate regions and the oceans are also vast storehouses of biodiversity, about which extremely little is known. Some examples of drugs from temperate zones include: aspirin, originally extracted from the willow tree (*Salix alba*); digitalis in the forms digoxin and digitoxin, still the main treatment for increasing cardiac contractility in heart failure, from the foxglove plant (*Digitalis purpurea*); and taxol from the Pacific Yew tree (*Taxus brevifolia*). Taxol provides an important example of the potential consequences of

our squandering species in our own backyard, as it was discovered through the National Cancer Institute's screening program for new drugs with anticancer activity in the bark of the Pacific yew, a tree that had originally been discarded during commercial logging in old growth forests of the Pacific Northwest. Original reports showed taxol able to induce remission in 30% of advanced ovarian cancer cases that had been unresponsive to other treatment (McGuire et al. 1989). While some of the initial excitement about taxol as the new cancer wonder drug has waned, it remains an important new advance in cancer chemotherapy and may still be the most promising medication known for the treatment of ovarian and breast cancer (Nicolaou et al. 1996).

Other potential new medicines from temperate organisms that hold great promise include a substance, betulinic acid, from the bark of the white birch, which in laboratory tests has demonstrated marked activity in reducing malignant melanomas (*New York Times* 3/28/95), and salivary anticoagulants from leeches, ticks, blackflies, and other organisms (Bang 1991), which may lead to powerful new anticoagulants.

The oceans, the original home for life on this planet, have barely been explored for new drugs. One on the market, known as cytarabine or ara-C, comes from the Caribbean sponge (*Tethya crypta*), and is one of the most effective agents known for inducing remissions in cases of acute myelocytic leukemia in children and adults (Calabresi and Chabner 1990). Another, bryostatin 1, from the bryozoan *Bugula neritina*, has shown a great deal of promise in Phase 1 trials for inhibiting tumor growth (Prendiville et al. 1993, Philip et al. 1993). Finally, a group of substances called pseudopterosins, extracted from the Caribbean Sea Whip (*Pseudopterogorgia elisbethae*), have been demonstrated to possess anti-inflammatory and analgesic properties more potent than currently available nonsteroidal anti-inflammatory agents such as indomethacin, through mechanisms that have yet to be defined (Look et al. 1986).

Loss of Medical Models

With a loss of species, we are also losing valuable medical models that may help us understand human physiology and disease. Several examples follow.

Dart-poison frogs, the *Dendrobatidae*, from the lowland tropical forests in Central and South America are fast disappearing as they are particularly vulnerable to deforestation (Myers and Daly 1983). Each of the 100 or so species occupies a very specific location in the rainforest and cannot live naturally anywhere else. They are enormously useful to medicine. These

frogs produce some of the deadliest natural toxins known, which have been used for centuries by native Indians to poison arrows and blowgun darts. The active ingredients are alkaloids, and it has been discovered that the reason for their extreme toxicity is that they bind selectively to sodium and potassium channels, calcium pumps, and acetylcholine receptors in nerve and muscle membranes, resulting in paralysis (Albuquerque et al. 1988). One of the toxins, batrachotoxin, for example, binds to a specific site in sodium channels and has been used increasingly by neurophysiologists to understand the structure and function of this most fundamental cellular unit, and to comprehend how nerves and muscles transmit electrical impulses (Albuquerque et al. 1971). If rainforest destruction continues at its present rate, these extremely valuable frogs could be lost.

In many parts of the world bears are also endangered, because of hunting and destruction of their habitats, but in particular, because of the very high prices their body parts bring on the Asian black market for use in traditional medicines and as gourmet food. Bear gallbladders are worth 18 times their weight in gold. The irony is that in medical terms, living bears are worth far more than the sum of all their body parts.

Hibernating, or more accurately denning, bears are biological wonders. Though largely immobile for 4 to 5 months or more, they do not lose bone mass (Floyd et al. 1990). A similar period of immobility or lack of weight bearing results in humans losing one-quarter or more of their bone mass—seen in bedridden and paralyzed patients, in astronauts, and in the inactive elderly. Understanding how bears prevent bone loss during immobility (the only vertebrate that can do this) could lead to ways of preventing or treating osteoporosis, a largely untreatable condition afflicting 25 million Americans, resulting in 1.5 million bone fractures and 50,000 deaths annually (*New York Times* 11/20/94), and costing the U.S. economy $10 billion dollars in direct health care costs and lost productivity each year (National Osteoporosis Foundation 1993).

Bears also do not urinate for the months of denning, as they are somehow able to recycle their urea to make new proteins (Nelson 1987, 1989). Humans, by contrast, unable to excrete their urinary wastes, die after a few days. If we understood how bears accomplished this feat, we might be able to find effective long-term treatments for those with chronic renal failure, who are now totally reliant on dialysis. Renal failure in the United States costs another $7 billion annually, a figure expected to increase to $10 billion by the year 2000 (*New York Times* 11/4/93).

Sharks are also being lost in record numbers from overfishing, and as a result we may never discover why sharks rarely develop tumors or infections, presumably the culmination of 400 million years of successful evo-

lution (Stevens 1992). Some clues have been discovered—MIT researchers have isolated a substance from one shark species, the Basking shark (see page 19), that strongly inhibits the growth of new blood vessels toward solid tissue tumors, thereby preventing their growth (Lee and Langer 1983). This and other work on angiogenesis-inhibiting factors offers one of the best new hopes for developing effective chemotherapeutic agents for some malignant tumors.

Another group of researchers has recently isolated a compound they named squalamine from the tissues of the dogfish shark. Squalamine has demonstrated extremely potent activity in lab tests against a variety of bacteria, fungi, and parasites through mechanisms not yet understood, but that seem entirely different from those of all other known antibiotics (Moore et al. 1993). As infectious agents are developing growing resistance to currently used antibiotics, the search for new drugs working through different pathways becomes increasingly important.

Predatory cone snails of the genus *Conus*, comprising approximately 500 species and found in tropical reef communities, produce a wide variety of toxins to capture their prey. These toxins are small peptides that act on voltage-sensitive calcium channels, sodium channels, *N*-methyl-D-aspartate (NMDA) receptors, nicotinic acetylcholine receptors, and vasopressin receptors in neuromuscular systems (Olivera et al. 1990). They have been increasingly used to understand the molecular structure of these channels and receptors and how they work, to provide clues for the mechanism of action of various human disease conditions, and to find new treatments for these conditions. Calcium channel antagonists derived from *Conus* toxins, for example, have been shown to help alleviate the exaggerated pain responses in some peripheral nerve lesions (Chaplan et al. 1994) and to differentiate the paraneoplastic neuromuscular transmission disorder, Lambert-Eaton syndrome, associated with small-cell lung carcinomas (Lennon et al. 1995) from myasthenia gravis (Miljanich and Ramachandran 1995). The laboratory findings that calcium channel toxins from cone snails also have the potential to prevent neuronal degeneration following focal (Takizawa et al. 1995) and global (Valentino et al. 1993) cerebral ischemia have generated the greatest interest, as these compounds may someday be used to limit nerve cell death in cases of bypass surgery, head trauma, cardiac arrest, and strokes (Miljanich and Ramachandran 1995).

Pit vipers (family *Crotalidae*, which includes rattlesnakes, cobras, and water moccasins) have also become invaluable to medical science. In the 1960s, it was discovered that pit viper venom contained compounds that were lethal to prey because they intensified the animal's response to

bradykinin (Ferreira 1965), a potent vasodilating substance, and thereby caused fatal hypotension. These bradykinin-potentiating factors were shown to be a family of peptides that inhibited kininase II, an enzyme that inactivates bradykinin. Kininase II was subsequently demonstrated to be the same enzyme as angiotensin converting enzyme (ACE), which catalyzes the conversion of angiotensin I, a relatively inactive substance, to angiotensin II, a powerful vasopressor (Garrison and Peach 1990). This understanding of the renin–angiotensin system and of the role of bradykinin gleaned from understanding the action of pit viper venom as an ACE inhibitor led to the development of a whole class of synthetic ACE inhibitors that have become some of the most effective agents known for treating hypertension.

The sea squirt, the only animal besides human beings to form stones naturally in their kidney-like organs, has been used to understand the mechanisms of how kidney stones and gout develop in humans. By studying the formation of both uric acid and calcium oxalate stones in one type of sea squirt, the sea grape (*Molgula manhattensis*), Mary Beth Saffo of the University of California at Santa Cruz is trying to develop strategies for preventing and treating these conditions (Yoon 1994).

The discovery of a new bacterial species, *Thermus aquaticus* (from thermal springs in Yellowstone National Park), which lives at extremely high temperatures (70–75°C) (Brock and Freeze 1969), led to the isolation of polymerase enzymes that have revolutionized DNA and RNA research (Air and Harris 1974) and to countless other applications, including the identification of criminals through their DNA.

Finally, the horseshoe crab (*Limulus polyphemus*), an animal which first evolved 350 million years ago, has proved invaluable in two areas of biomedical research. The first concerns work on vision. Because the horseshoe crab possesses one of the largest and most accessible optic nerves in the animal kingdom, and has the largest photoreceptors of any animal, it has been extensively studied to help understand the fundamental mechanisms of animal vision, and of the way the brain interacts with sensory organs (Hartline et al. 1956, Barlow 1990), insights that may lead to a greater understanding of human vision. The second concerns diagnostic bacteriology. As a result of early discoveries by Frederik Bang on the *Limulus'* clotting response to injections of gram negative bacteria (Bang 1956), the processed blood from the crab, *Limulus* amoebocyte lysate, has developed into one of the most sensitive tests available to detect the presence of gram negative endotoxins. It was because of this test that batches of swine flu vaccine were first shown to be contaminated in the mid 1970s (Sargent 1987).

There are countless other examples of unique microorganisms, plants, and animals holding the secrets of hundreds of millions of years of evolution and hundreds of billions of biological experiments, which, because of species extinctions, are in danger of being lost forever to medical science.

Infectious Diseases

It is important to discuss how alterations in biodiversity can disrupt ecosystem equilibria resulting in the emergence or reemergence of infectious diseases in man. This may be one of the most serious public health consequences of biodiversity loss; it is also perhaps one of the most neglected and poorly understood.

The case of the hantavirus outbreak in the United States serves as a valuable model illustrating the potential effects of such alterations, as well as our relative lack of knowledge about infectious agents in the environment, and the processes that uncover them. Other cases will be discussed more fully in Chapter 2.

Six years of drought in the Four Corners Area of the American Southwest, where Utah, Colorado, Arizona, and New Mexico meet, ended in the late winter and spring of 1993 with unusually heavy snows and rains (Wenzel 1994). These dramatic weather patterns, seen in other parts of the world as well and thought to result directly from an intense and prolonged El Niño (and perhaps indirectly from greenhouse gas-induced warming of the seas), resulted in a superabundance of piñon nuts and grasshoppers, food for the native deer mouse. At the same time, the drought had led to a reduction in the mouse's predators—foxes, snakes, and owls, and as a result, the mouse population exploded, increasing tenfold by May of 1993 over levels of the year before (Wenzel 1994). Deer mice, it was subsequently learned, carry a hantavirus that they shed through their saliva and excreta, and as a consequence of greatly increased exposure by people in the area to the huge mouse population, an epidemic of a rapidly fatal respiratory syndrome developed—17 previously healthy people, most of them Native Americans, initially got the disease; 13 died (Duchin et al. 1994). The number of confirmed cases of hantavirus pulmonary syndrome in the United States has reached 131 in 24 states, mostly in the West, of which almost one-half have been fatal (Freeman 1996).

Other examples of changes in habitats and biodiversity associated with infectious disease spread include Kyasanur Forest Disease, a tickborne hemorrhagic viral disease identified in Mysore, India and linked to deforestation in that region (Morse 1991); Argentine Hemorrhagic Fever, a viral illness carried by a mouse which proliferated and spread with the clearing of the pampas grasslands in Argentina for the purpose of growing corn (Morse 1990); and malaria in the Amazon which has reached epidemic proportions in the past 20 years (Kingman 1989), as a result of forest clearing and the creation of large numbers of still pools where *Anopheles darlingi*, the most important malaria mosquito vector in the area, can multiply unchecked (Walsh et al. 1993). It is not clear whether the recent cases of locally acquired malaria in the United States (Brook et al. 1994, Bell et al. 1995) (which hadn't been seen in 50 years) are also the result of habitat changes, secondary to the unusually warm summers of the past several years which favored the proliferation of native mosquitoes and the transmission of malaria, originally acquired abroad.

These cases illustrate how fragile and complex the equilibria among species in ecosystems are, how little we understand these equilibria, and how a loss of biodiversity (in some cases through changes in weather, but in other cases, perhaps through habitat destruction, the direct elimination of predators, stratospheric ozone depletion, or other means) may result in potentially catastrophic consequences for human beings. No one knows how many viruses or other infectious agents in the environment, potentially harmful to man, are now being held in check by the natural equilibria afforded by biodiversity.

Conclusion

Global climate change, stratospheric ozone depletion, toxic substances released into the environment, and habitat destruction all have the capacity to lead to species extinction and biodiversity loss. Current rates of species loss from human activity rival the great geologic extinctions of the past. With a loss of biodiversity, we risk losing potential new medicines to treat human illnesses that are presently untreatable, foreclosing the possibility of discovering valuable medical models that may help us understand human physiology and disease, and disrupting ecosystem balances on which all life, including human life, depends.

The fundamental relationship between biodiversity and human health is generally unappreciated by policymakers and the public, and as a result, the preservation of habitats and of species is given a low priority. In addition, there is little understanding that the study of species and of biodiversity may offer the best means we have for predicting future dangers to human

beings from environmental degradation, as some species may be affected at lower thresholds to environmental hazards than we are and serve as our "canaries," or so-called "indicator species."

How can the importance of biodiversity become central to the concerns of policymakers and the public? There is a lesson to be learned from the history of chlorofluorocarbons and the ozone layer. Once the magnitude of the danger was clear, and the consequences to human life were obvious, then the world community was able to take effective action to protect the ozone layer. The same must occur with the issue of biodiversity—it is essential that people understand that their health and lives, and those of their children, depend so completely on the health of other species and of global ecosystems. Only then will they develop the motivation to support personal behaviors and public policies that protect biodiversity. There is no task more important for physicians, other health professionals, scientists, and concerned citizens than helping to promote this understanding.

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Global Climate Change and Emerging Infectious Diseases

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Climatic factors influence the emergence and reemergence of infectious diseases, in addition to multiple human, biological, and ecological determinants. Climatologists have identified upward trends in global temperatures and now estimate an unprecedented rise of 2.0°C by the year 2100. Of major concern is that these changes can affect the introduction and dissemination of many serious infectious diseases.

The incidence of mosquito-borne diseases, including malaria, dengue, and viral encephalitides, are among those diseases most sensitive to climate. Climate change would directly affect disease transmission by shifting the vector's geographic range and increasing reproductive and biting rates and by shortening the pathogen incubation period. Climate-related increases in sea surface temperature and sea level can lead to higher incidence of water-borne infectious and toxin-related illnesses, such as cholera and shellfish poisoning. Human migration and damage to health infrastructures from the projected increase in climate variability could indirectly contribute to disease transmission. Human susceptibility to infections might be further compounded by malnutrition due to climate stress on agriculture and potential alterations in the human immune system caused by increased flux of ultraviolet radiation.

Analyzing the role of climate in the emergence of human infectious diseases will require interdisciplinary cooperation among physicians, climatologists, biologists, and social scientists. Increased disease surveillance, integrated modeling, and use of geographically based data systems will afford more anticipatory measures by the medical community. Understanding the linkages between climatological and ecological change as determinants of disease emergence and redistribution will ultimately help optimize preventive strategies.

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EMERGING and reemerging infectious diseases are defined as those increasing in incidence in the recent past or threatening to increase in the near future.[1,2] The entry and subsequent establishment of a pathogen into a new human population must occur for a disease to emerge successfully,[3] and multiple factors with complex interactions are often involved. Climatic conditions play a role in such dynamics, and climatologists have recently identified an accelerated change in long-term global climate trends.[4-10] The assessment of the potential health impacts of these changes now requires evaluation by the medical community.

Many newly emerging diseases in humans are actually long-standing zoonoses of animal host species that surface in human populations after a climatic or environmental change.[2] For example, the pulmonary *Hantavirus* epidemic in the southwest United States was felt to be due to an upsurge in rodent populations related to climate and ecological conditions.[11] Six years of drought, followed by extremely heavy spring rains in 1993, resulted in a 10-fold increase in the population of deer mice, which are the known reservoir of *Hantavirus*.[12,13]

In sub-Saharan Africa, meningococcal meningitis follows a distinct seasonal pattern. Epidemics consistently erupt during the hot dry season and subside soon after the onset of the rainy season.[14] In Nigeria during 1977 through 1979, peak meningitis incidence was strongly correlated with the highest mean maximum temperatures of the season and inversely correlated with absolute humidity to a lesser extent, though still significantly.[15]

In addition to climatological or environmental factors, determinants for emergence include biological, cultural, technological, and socioeconomic factors.[1,3] Changing climate conditions substantially could affect many of these determinants. This article focuses on the more direct effects of climate change on vector and parasite biology and distribution; however, climate's indirect effects on regional food supply and human migration patterns may substantially alter susceptibility to infectious agents.

Assessing how changing climate conditions can alter the life cycles of vectors and parasites is especially critical in understanding the processes behind the emergence or reemergence of many diseases. Diseases in which infectious agents cycle through cold-blooded (invertebrate) species to complete their development are particularly sensitive to subtle climate variations[16,17] compared with diseases spread from human to human. Climate factors strongly determine vector infectivity by affecting pathogen replication, maturation, and the period of infectivity.[18,19] Extreme heat, on the other hand, can shorten insect survival time or disrupt pathogen development.[20]

The geographic range of many vector-borne diseases is limited by climate parameters. For example, the range of the dengue fever vector, the mosquito *Aedes aegypti*, is limited by freezing temperatures that kill overwintering eggs.[21,22] Work by the US National Climatic Data Center demonstrates that minimum temperatures are increasing at a disproportionate rate compared with average and maximum temperatures,[23] and this trend is predicted to continue under climate change scenarios.[5,6] Such conditions may allow parasites and their vector or reservoir hosts to extend into regions previously void of disease.

CLIMATE CHANGE: OBSERVATIONS, PROJECTIONS, AND UNCERTAINTIES

Greenhouse gases (GHGs) allow sunlight to penetrate to the earth's surface, yet prevent infrared radiant heat from escaping. The major anthropogenic GHG is carbon dioxide (CO_2), but methane, nitrous oxide, and chlorofluorocarbons also contribute to radiative climate forcing (warming) by human activity.[10] Fossil fuel emissions and deforestation are the main causes of increasing atmospheric CO_2 (trees sequester carbon and serve as a CO_2 "sink"). Levels of CO_2 have risen by

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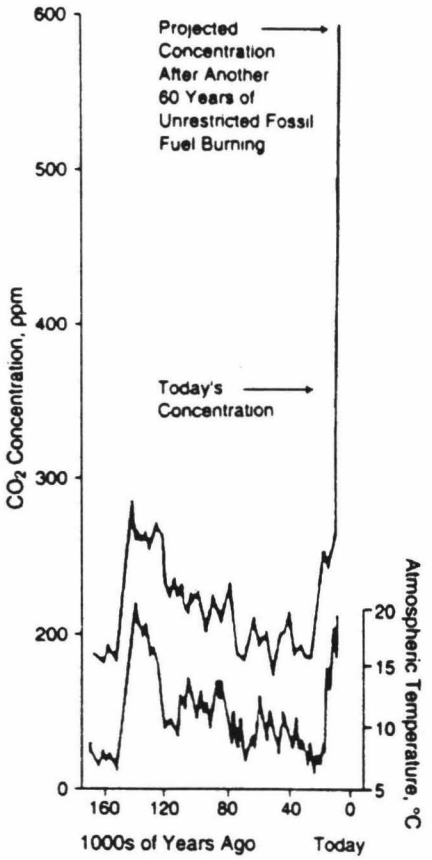


Figure 1.—Global average temperatures (lower line) and carbon dioxide (CO_2) concentration (upper line), 158 000 BC to 1994 AD as determined from Antarctic ice core records (adapted and reprinted with permission from Flavin[26]).

29% (from 278 ppmv to 358 ppmv) since the industrial revolution.[24,25]

Historical records indicate a direct correlation between atmospheric CO_2 levels and average global temperatures[26] (Figure 1). According to the United Nations Intergovernmental Panel on Climate Change, anthropogenic GHG emissions are significantly accelerating current warming trends, which have now been determined to be inconsistent with natural climate variation.[6-8] The global mean surface air temperature has increased approximately 0.5°C over the last 100 years.[5,10] Sea level also has risen by 1 to 2 cm per decade due to climate-related factors, eg, oceanic thermoexpansion and melting of mountain glaciers, as opposed to land subsidence.[27] Mountain snow cover has decreased[6] and oceanographers have recently documented statistically significant deep ocean warming during the period from 1957 through 1992.[28]

The mid-range estimates of future temperature change by the year 2100 are 2.0°C (range, 1.0°C to 3.5°C),[5] or 0.2°C per decade.[9] These figures assume some reduction in the rate of economic growth, plateauing of population rise by the middle of the next century, and an increase in conservation measures. Even if extensive action is immediately taken to reduce GHGs, global temperatures are expected to continue to warm by 0.5°C to 2.0°C by the year 2100.[5,10] Such climate sensitivity to GHG accumulation is consistent with paleontologic data extending over 150 000 years. Mid-value estimates for sea level rise approximate 50 cm by the year 2100.[10,29] This projected rise in both temperature and sea level represents a respective fivefold and threefold faster rate than that observed over the past century.[10,29]

Though model predictions show much agreement, many uncertainties still persist. Major issues include the following: (1) cloud formation from increasing water vapor—depending on altitude, clouds may reflect sunlight (cool) or further insulate (warm); (2) ocean heat capacity—predicting the effect of ocean currents as a buffer to surface warming is still unresolved; (3) sulfate aerosols that cause regional cooling—the most recent climate models now cited by the Intergovernmental Panel on Climate Change are now accounting for these aerosols; (4) CO_2 fertilization of plants—CO_2 enhances photosynthesis in plants increasing their absorption of CO_2, a feedback that potentially could dampen the rise in atmospheric concentrations; (5) the carbon cycle—full accounting for the fate of CO_2 emissions reveals uncertainty in the magnitude of the carbon sink.[10,30] Regarding applications to health, most global climate models do not provide fine enough resolution to predict local conditions that may be pertinent to specific diseases.

While these uncertainties may remain elusive, there is increasing convergence of climate projections arising from independent efforts using diverse methodologies. The medical community is beginning to explore what these predictions might mean for public health. The World Health Organization considers the health ramifications of global warming as one of the largest public health challenges for the upcoming century.[31,32]

VECTOR-BORNE AND WATER-BORNE DISEASES

Changing trends in average temperature and precipitation are anticipated to have an impact on vector-borne disease incidence and distribution. Diseases expected to be affected by climate change are listed in Table 1 from the World Health Organization.[31] The following sections will illustrate how some of the major mosquito-borne diseases may extend or intensify with climate change. They include (1) malaria; (2) dengue and dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS); and (3) arboviral encephalitides. Water-borne diseases associated with temperature-sensitive marine ecosystems will also be addressed, and include (4) cholera, found to be harbored by zooplankton; and (5) toxic, rather than infectious, algae (red tides).

Direct Effects on Specific Reemerging Diseases

Malaria.—Malaria is the most prevalent vector-borne disease globally and causes 1 million to 2 million deaths annually.[33] A marked resurgence of malaria has occurred since 1973,[34] and according to the Institute of Medicine, efforts to control malaria have been disappointing. More than 50 mosquito species have developed resistance to insecticides since 1947.[35] Drug resistance persists for the most virulent species, *Plasmodium falciparum*, and antimalarial vaccines have shown only limited efficacy.[33,36,37] In many regions where malaria transmission had been almost eliminated, the disease has made a comeback, sometimes surpassing earlier recorded levels.[33]

Malaria generally extends to the 16°C winter isotherm, since parasite development does not occur below this temperature.[34,38] Temperature and humidity are among the most important factors for disease transmission and the extrinsic incubation period (EIP) of the parasite shortens dramatically at temperatures between 20°C and 27°C.[20,34] The EIP is defined as the number of days between the vector's ingestion of an infected blood meal and the point that it becomes capable of transmitting infection. Climatic factors that increase the inoculation rate of *Plasmodium* pathogens, as well as the breeding activity of *Anopheles* mosquitoes, are considered the most important cause of epidemic outbreaks of malaria in nonendemic areas.[34]

Malaria incidence related to local climatic change has been observed in Rwanda, when in 1987, extension of malaria into higher altitudes resulted after record high temperatures and rainfall.[39] Monthly malaria incidence in high-altitude regions was exponentially affected by changes in minimum temperature. In low-altitude zones, rainfall and mean temperature were the most significant climatic factors. In Zimbabwe, temperature defines malaria distribution as well, since malaria incidence and prevalence are strongly linked to altitude (Figure 2).[40]

Based on such observations, a relatively small increase in winter (minimum) temperature would likely facilitate the spread of malaria into large urban highland populations that are currently malaria-free and immunologically naive, such as Nairobi, Kenya, and Harare, Zimbabwe. According to malaria models under climate

Status of Major Vector-borne Diseases and Predicted Sensitivity to Climate Change*

Disease	Populations at Risk, Millions†	Prevalence of Infection, Millions‡	Present Distribution	Possible Change of Distribution as a Result of Climatic Change
Malaria	2100	270	Tropics, subtropics	Highly likely
Lymphatic filariases	900	90 2	Tropics, subtropics	Likely
Onchocerciasis	90	17 8	Africa, Latin America	Likely
Schistosomiasis	600	200	Tropics, subtropics	Very likely
African trypanosomiasis	50	25 000 new cases per year	Tropical Africa	Likely
Leishmaniasis	350	12 million infected + 400 000 new cases per year	Asia, southern Europe, Africa, South America	Not known
Dracunculiasis	63	1	Tropics (Africa, Asia)	Unlikely
Arboviral diseases				
Dengue			Tropics, subtropics	Very likely
Yellow fever			Africa, Latin America	Likely
Japanese encephalitis			East and Southeast Asia	Likely
Other arboviral diseases			Tropical to temperate zones	Likely

*Data from World Health Organization.[31]
†Based on a world population estimated at 4.8 billion (1989).
‡Ellipses indicate no estimates available.

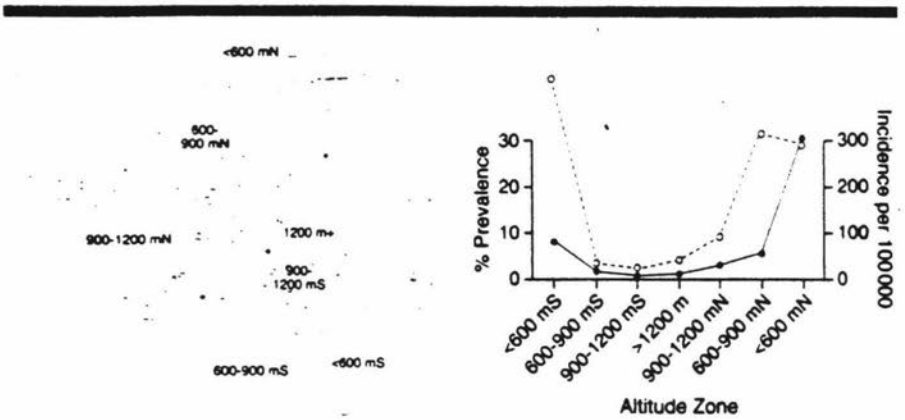


Figure 2.—Left, altitude classification of Zimbabwe and, right, average annual malaria prevalence (solid line) and incidence (dotted line) per 100 000 population by altitude zone; mS indicates meters, South; m, meters; mN, meters, North; and m+, 1200 meters and higher. Prevalence data are from 1969 through 1981 and incidence data are from 1972 through 1981 (adapted and reprinted with permission from Taylor and Mutambu[40]).

change scenarios,[41,42] risk of malaria epidemics would rise substantially in both tropical and temperate regions. An estimated 1 million additional fatalities per year could be attributed to climate change by the middle of the next century, according to one model.[43]

Dengue and Dengue Hemorrhagic Fever/Dengue Shock Syndrome.—Globally, 520 arthropod-borne viruses, or arboviruses, have been identified, of which over 100 can produce human disease.[2,44] Dengue and yellow fever are due to flaviviruses and share the same principal mosquito vector, *Ae aegypti*. Urbanization, inadequate mosquito control, absence of water systems, and international travel or migration are major factors leading to the reemergence of dengue.[45,46] Climate conditions, however, contribute to epidemic spread and geographic distribution.[47,48]

Dengue, or "breakbone fever," is a severe viral illness occurring sporadically and in epidemics.[49] Unlike yellow fever, there is no vaccine or antiviral pharmaceutical available for dengue. Outbreaks in urban areas infested with *Ae aegypti* may be explosive, with up to 70% to 80% of the populations involved.[50] In the 1950s, the more severe DHF/DSS appeared in Southeast Asia, and is thought to be caused by sequential infection by any two of the four serotypes of the dengue virus in hyperendemic locations.[51] Between 250 000 and 500 000 DHF/DSS cases occur yearly throughout the world, and case fatality rates approach 40% to 50% if untreated,[44] and 1% to 5% with appropriate fluid replacement therapy.[52] Since the late 1970s dengue has reemerged and DHF/DSS has emerged in the Americas.[45,46,50]

Currently, dengue viruses are being transmitted in the tropics between 30° north and 20° south latitude,[53] since frosts or sustained cold weather kills adult mosquitoes and overwintering eggs and larvae.[22,54] Warming trends, therefore, can shift vector and disease distribution to higher latitudes or altitudes, as was observed in Mexico when dengue reached an altitude of 1700 m during an unseasonably warm summer in 1988.[55] Other epidemiological studies help confirm this relationship between dengue and temperature. During the 1978-1979 epidemic in Honduras, no endemic dengue occurred in Tegucigalpa, where average temperatures are 4°C cooler than the coastal lowlands.[56] In Mexico in 1986, the most important predictor of dengue prevalence was found to be the median temperature during the rainy season, with an adjusted fourfold increase observed between 17°C and 30°C.[57]

Temperature also affects the transmission dynamics of dengue. Warmer temperatures reduce larval size of *Ae aegypti*, ultimately affecting adult size.[58] Smaller adults must feed more frequently to develop an egg batch,[47,59] boosting the incidence of double feeding within each gonotrophic cycle.[47] This direct relationship between biting rates and temperature has been found in field studies from Thailand.[60] Regarding viral development, the EIP shortens with higher temperatures,[48,61] increasing the proportion of mosquitoes that become infectious at a given time.[62] For example, the EIP for dengue type-2 virus requires 12 days at 30°C and only 7 days at 32°C to 35°C.[61] Shortening the incubation period by 5 days translates to a potential threefold higher transmission rate of disease.[57] In short, slightly higher temperatures within the range of mosquito viability lead to more infectious mosquitoes that bite more frequently.

Arboviral Encephalitis.—Of reported encephalitis cases in the United States, 65% are of arboviral etiology.[63] Most are mosquito-borne and, in order of prevalence in the United States, include the following: St Louis encephalitis (SLE) and La Crosse encephalitis, and western, eastern, and Venezuelan equine encephalomyelitis. Clinical features of the most common North American pathogenic arbovirus, SLE, range from headache to aseptic meningitis and encephalitis, with the elderly at highest risk for mortality. Epidemics generally occur south of the 20°C June isotherm, but northerly outbreaks have occurred during unseasonably warm years.[63]

Several vector species exist for SLE: *Culex tarsalis* in the rural west where SLE is endemic, *Culex nigripalpus* in Florida, *Culex pipiens quinquefasciatus* in the urban southeast, and *Culex pipiens pipiens* in the urban north.[63] Human outbreaks of SLE are highly correlated with several-day periods when temperature exceeds 30°C (85°F),[64] as was the case during the 1984 California epidemic that followed a period of extremely

high temperatures. Precipitation patterns are also important for transmission.[66] Computer analysis of monthly climate data has demonstrated that excessive rainfall in January and February, in combination with drought in July, most often precedes SLE outbreaks.[66] Such a pattern of warm, wet winters followed by hot, dry summers closely resembles the computer global circulation model projections for climate change in the United States.[4,5,67]

From field studies in California, a 1°C increase in temperature corresponds to a 1% decrease in adult mosquito mean daily survivorship.[68] Offsetting this potential benefit, viral transmission rates rise sharply at higher temperatures (Figure 3).[69,70] From their results, Reeves et al, predict that a 3°C to 5°C temperature increase will cause a significant northern shift in both western equine encephalitis and SLE outbreaks, with disappearance of western equine encephalitis in southern endemic regions.

Other Vector-borne Diseases.—Schistosomiasis has increased in prevalence in arid warm regions primarily from expansion of irrigation systems where snails serve as the intermediate host. Water shortages predicted for many agricultural areas could thus potentiate further risk in these regions by increasing demand for irrigation. Also, warmer temperature influences infectivity and development of the parasite within the snail. During winter, cercarial infection in water snails becomes dormant and potential transmission sharply diminishes.[71,72] Therefore, if temperatures increase, snails could spread schistosomiasis over a longer period during the year.[31,73] Recent modeling of schistosomiasis predicts an additional 5 million cases attributed to climate change by the year 2050.[74]

Onchocerciasis, or "river blindness," is a blackfly-borne disease primarily found in West Africa and, to a lesser extent, in Latin America. Climate plays an important role in the occurrence of onchocerciasis since the vector requires fast-flowing water for successful reproduction, and the adult vector can be spread by wind.[75] A recent study found that if temperature and precipitation change across portions of West Africa as predicted by some global circulation models, blackfly populations may increase by as much as 25% at their current breeding sites.[76] Potential abandonment of agricultural land in river valleys could add to regional food production problems.

African trypanosomiasis, or "sleeping sickness," is carried by tsetse flies, whose distribution depends on vegetation cover. Researchers in sub-Saharan Africa have correlated vegetation type to the population densities of tsetse flies using satellite images to predict a large extension of regions at risk for this disease, assuming a 3°C mean monthly temperature rise.[77,78]

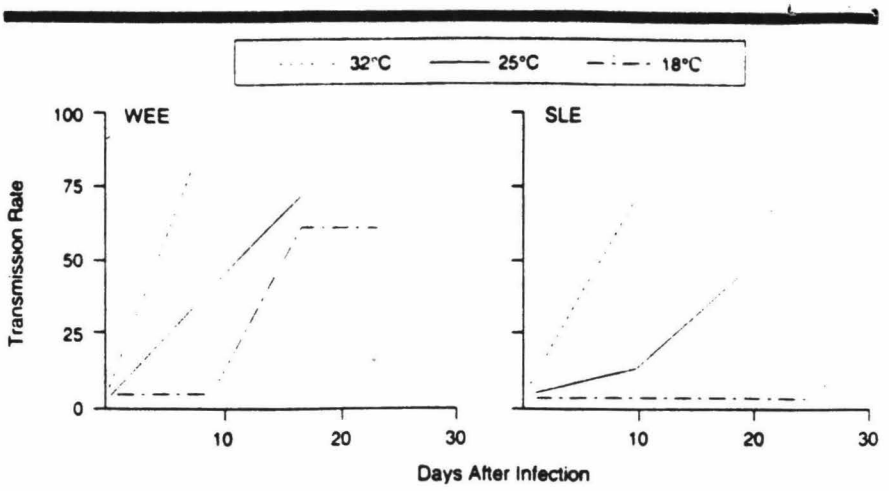


Figure 3.—Effect of temperature on transmission rates (the percentage of bites that result in transmission) of Western equine encephalitis (WEE) and St Louis encephalitis (SLE) viruses by the mosquito, *Culex tarsalis* (reprinted with permission from Reeves et al[69]).

Tick-borne diseases are also sensitive to climatic conditions but favor cooler temperatures. In Africa, Rogers and Randolph found mean monthly maximum temperature to be the strongest predictor of tick occurrence at the margins of endemic zones.[79] Only 2°C determined the difference between areas where ticks are present or absent in southeastern Africa. In the southern United States, Rocky Mountain spotted fever may decline due to ticks' intolerance of high temperatures and diminished humidity.[80]

Cholera and Toxic Algae

During the past decade, phytoplanktologists have reported an unusual spread and intensity of algal blooms worldwide.[81] Increases in phytoplankton (or algae) globally have been a consequence of wetland loss, poor erosion control management, liberal agricultural application of fertilizers, and coastal sewage release, all resulting in effluents rich in nutrients that promote algae growth. These growth-favoring factors could be augmented by warmer sea surface temperatures expected with global climate change.

Over the past century, average sea surface temperature has increased approximately 0.7°C,[3] and marine growth of algae has been observed to respond to localized temperature increases in nutrient-replete waters. For example, one species of toxic phytoplankton previously confined to the Gulf of Mexico, *Gymnodinium breve*, extended northward in 1987 after a "parcel of warm gulf stream water" reached far up the East Coast resulting in human neurological shellfish poisonings and substantial fishkills.[82] Red tides, which cause paralytic shellfish poisoning, diarrheic shellfish poisoning, and amnesiac shellfish poisoning are blooms of toxic dinoflagellates. Warm water favors the growth of dinoflagellates and cyanobacteria that include more toxic organisms.[83]

Zooplankton, which feed on algae, can serve as reservoirs for *Vibrio cholerae* and other enteric pathogens, particularly gram-negative rods.[84] Large coastal blooms may have contributed to the recent multi-epicentered cholera pandemic in Latin America. Using fluorescent antibody techniques, forms of quiescent *V cholerae* have been found to persist on the sheaths and exoskeletons of marine organisms that can revert to a culturable state when nutrients, pH, and temperature permit.[85]

In October 1991, algal paralytic saxotoxins were detected for the first time in Chilean waters as far south as the Straits of Magellan.[86] The unusual and prolonged extension into new areas led to approximately 300 cases of intoxication from shellfish, including 11 deaths. This southern extension, coinciding with the penetration of cholera into Latin America, lends credence to the hypothesis that coastal algal blooms were associated with the intensity and breadth of the current pandemic. Climatologists are beginning to question whether large-scale changes in marine ecosystems are already indicative of sea-surface warming due to the greenhouse effect.[87]

Extreme Weather Events and Climate Variability

In addition to sea level rise, more frequent extreme weather events are predicted to accompany global warming.[7,88] Severe storms can cause contamination of water systems and simultaneously create breeding sites for insects or favorable conditions for rodents that carry diseases. Destruction of shelters leaves human

populations more exposed to infectious vectors, increasing the potential for epidemics.

Human migration away from coastal, rural, or other economically or physically vulnerable locations could be anticipated. Many regions throughout the tropics and subtropics have been identified as being vulnerable to an increase in extreme weather events.[89] The potential risk of epidemics could increase in urban settings as refugees arrive from disease-endemic areas.[90,91] Already, current trends in urbanization increase the potential for disease epidemics such as cholera and dengue fever.

El Niño.—Some of the anticipated health impacts associated with extreme climate variability are already within the range of current human experience. Many disease outbreaks have been associated with the erratic weather conditions driven by El Niño Southern Oscillation (ENSO) events. ENSO is a climate phenomenon that is second only to seasonal cycles in its impacts on regional climate variability,[92] and occur on average every 4 years.[93] Anomalous fluctuations in precipitation, even to the extent of floods or droughts, are known to result from climate variations influenced by ENSO events.

Extreme heavy rainfalls have been correlated with outbreaks of Murray Valley encephalitis and Ross River virus in Australia, eastern equine encephalitis in the United States,[92] West Nile fever in southern Africa,[94] and cyclical malaria epidemics in Argentina[95] and Pakistan.[96] Such climate-related outbreaks have closely corresponded to ENSO cycles, which are now thought to be the driving force behind these geographically specific extreme climatic conditions.[97,98] Malaria can also be associated with droughts linked to ENSO phenomenon that create pools from rivers in Sri Lanka.[97] The agriculturally devastating drought in countries of the Indian Ocean region in the past several years has been attributed to a persistent El Niño, as well.[94]

These ENSO-related outcomes may serve as an analogue for analyzing repercussions from long-term changes in climate variability and extremes. Furthermore, some evidence suggests that ENSO events may become more frequent as the earth warms,[99,100] and variability in the incidence of vector-borne diseases will likely increase as a result of global greenhouse warming.[92]

INDIRECT EFFECTS ON HUMAN SUSCEPTIBILITY

Agriculture and Human Nutrition

Climate change could adversely affect agriculture both by long-term changes, such as reducing soil moisture through evapotranspiration, and more immediately, by extreme weather events such as droughts, flooding (and erosion), and tropical storms.[101] Sea level rise could affect food production through the combination of inundation and increased salinity of coastal farmlands.

On the other hand, "CO_2 fertilization" enhances photosynthesis and may initially benefit plants.[102] Accounting for this beneficial effect, a study involving 30 nations still estimated that 40 million to 300 million additional people worldwide could be at risk from hunger due to climate change.[103] This study adjusted for predicted international trade liberalization that would be expected to ameliorate regional food shortages. The potentially large impact of changing distribution of plant pests and pathogens is a relative unknown.

Ultraviolet-Induced Immunosuppression: Potential for Synergism?

Stratospheric ozone depletion, accompanied by increases in ambient, biologically destructive ultraviolet-B radiation,[104] may exacerbate the effect of climate change on infectious diseases. Arising from a different anthropogenic process than climate change, ozone destruction is occurring primarily from reactions between ozone and halogen free radicals derived from chlorofluorocarbons, other halocarbons, and methyl bromide.[105] In addition to causing skin cancer and cataracts,[105,107] ultraviolet light has been shown to cause immunosuppression in both animal and human studies.[105,108-114] Ultraviolet-B radiation impairs antigen processing and presentation by Langerhan cells at the local level,[115-117] as well as altering lymphokine production, which reduces T-helper and T-suppressor cell ratios at the systemic level.[118-122]

Exposure can affect the course of infectious diseases of the skin such as onchocerciasis and dermatophytosis, and diseases where the skin is a portal of entry, as in leishmaniasis.[123] A recent human study found ultraviolet radiation to impair granulomatous delayed-type hypersensitivity response to leprosy antigens, suggesting the potential for ultraviolet-related impaired defense against intracellular pathogens.[109] In short, increased ultraviolet-B exposure may augment the potential for disease emergence and dissemination by lowering human immune defenses.

CONCLUSION AND RECOMMENDATIONS

To facilitate primary prevention of emerging infectious diseases, greater predictive capability needs to be developed. This will require new, interdisciplinary methods of analysis and response strategies. Unlike classical epidemiological focus on attack rates and human populations, understanding emerging infectious diseases will require a broader focus on ecosystem dynamics, including climate variables, habitat characteristics, and host and vector species populations, aside from human disease parameters.[124-126] Mathematical models have recently been developed that integrate many of these variables in an attempt to predict disease incidence.[41,42,74,127]

An essential step in recognizing and thereby mitigating the emergence of infectious diseases is enhanced surveillance and response. Attention needs to be directed toward establishing sentinel diagnostic centers in sensitive geographic regions bordering endemic zones.[89] Such detection will not only provide an early warning for possibly more pervasive changes in disease behavior and allow for intervention, but will also enrich our knowledge of climate-related diseases and facilitate the creation of better predictive models.

In September 1995, the US National Academy of Sciences, the Institute of Medicine, and the National Science and Technology Council cosponsored an international conference on "Human Health and Global Climate Change." Currently, the National Academy of Sciences and the Institute of Medicine are jointly considering undertaking a comprehensive interdisciplinary study of the relationship between climate and infectious diseases.

The diseases mentioned in this article help illustrate the linkages between climate, ecosystems, and human health. Better understanding of these relationships will require new analytical tools and cooperation between physicians on the one hand, and climatologists, biologists, and social scientists on the other.[128] Examples of useful analytical tools include geographic information systems to organize geographically based disease, climate, and demographic data, and remote satellite sensing technology that provides valuable data on land use patterns, habitat characteristics, and marine ecosystems.[129] In recent studies, geographic information systems and satellite-generated vegetative index maps were used to identify areas receptive to dengue fever and Lyme disease in the United States, schistosomiasis in Egypt and the Philippines, and malaria in temperate rice-growing regions.[129,130]

Disease emergence and reemergence have multiple determinants. Climate variables can influence disease processes at varying levels, from directly affecting pathogen maturation and vector reproduction, to altering vector or host habitats, human nutrition, and human demographics. Global climate change can alter the distribution of infectious diseases,

placing new and potentially large human populations at risk. Many of the impacts of climate change may become evident only over an extended period, given the inertia of the climate system. Alternatively, some of the recent examples of emerging infectious diseases may already reflect early changes in long-term trends of climatic means and/or variability. In either case, the potential impacts of climate change on the sustainability of public health combined with the difficulty of reversing ecosystem changes once they have occurred, warrant increased efforts by the medical community in addressing this problem in a concerted and timely fashion.

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Look to Weather for Clues to Malaria Comeback

To the Editor:

"Malaria Makes a Comeback, and Is More Deadly Than Ever" (front page, Jan. 8) captures the multiple factors — population movements, chemical resistance, lapsed public health vigilance and environmental change — influencing the resurgence of malaria. Mosquitoes, the transmitters of the disease, are indeed quintessential opportunists and adapt readily in disturbed environments.

As co-author of the World Health Organization report discussed in your article, I offer several recent findings. Consistent with model projections that global warming could hasten the geographic spread of malaria and dengue fever, these devastating diseases are now occurring at high altitudes in Latin America, central Africa and Asia. Cerebral malaria has occurred in Nairobi, Kenya, while dengue fever is found in the mountains around San José, Costa Rica.

Moreover, highland malaria and dengue fever are occurring in the context of upward migration of plants on many continents and summit glacial retreat in Latin America, Europe, central Africa and Asia. A recent study in the journal Nature confirmed that the freezing levels in the mountains have indeed shifted upward about 500 feet since 1970, representing a warming of close to 2 degrees Fahrenheit.

As we enter a year of debate concerning climate change (the convention will be held in Kyoto, Japan, in December), it is prudent to examine the potential consequences associated with continued warming and climate instability. Your article says that malaria "hinders economic development"; epidemics are growing ever more costly in terms of health, development, trade and tourism.



Lars Leetaru

While the resurgence of infectious disease has multiple social, biological and environmental roots, meteorological factors may play an increasing role in the future. We may be vastly underestimating the social and economic damages associated with epidemics and extreme weather events as well as the potential benefits to society as a whole of changing our environmental and energy policies.

PAUL R. EPSTEIN, M.D.
Boston, Jan. 8, 1997

The writer is associate director of the Center for Health and the Global Environment at Harvard Medical School.