SCIENCE

VOL. 96 FRIDAY, AUGUST 28, 1942 No. 2487

SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. MCKEEN CATTELL and published every Friday by

THE SCIENCE PRESS

Lancaster, Pennsylvania

Annual Subscription, $6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington, D. C.

MOSQUITOES, MALARIA AND THE WAR IN THE PACIFIC[1]

By EDWARD PHILPOT MUMFORD

OXFORD UNIVERSITY AND STANFORD UNIVERSITY

THE recent fall of Bataan was attributed mainly to malaria and lack of quinine by the United Press correspondent, Frank Hewlett, writing in *The New York Times* for April 18, and other observers. In the last war malaria took first place among the diseases responsible for casualties. Even in normal times, it is one of our most important public health problems. With the Dutch East Indies now largely in enemy hands, the principal source of supply of the world's quinine is lost to the United Nations, and although synthetic anti-malarials have been in use for some time, one can not overestimate the seriousness of a quinine shortage. Because of a low toxicity, and the fact that careful medical supervision is not required, quinine is still the most valuable drug for malarial prophylaxis and the treatment of acute malaria. There is no drug known to-day which can completely replace quinine and the other cinchona alkaloids. Because of these and other factors which are obvious, it is particularly important at this time to consider

[1] "Studies on Faunal Distribution," No. 7. These studies have received the support of the Carnegie Corporation of New York, the National Academy of Sciences, the American Association for the Advancement of Science, the Society of Sigma Xi, the American Philosophical Society, the May Esther Bedford Fund, Incorporated, and various subscribers to the Oxford University Chest. See G. D. Hale Carpenter, SCIENCE, 95: 325–326, 1942.

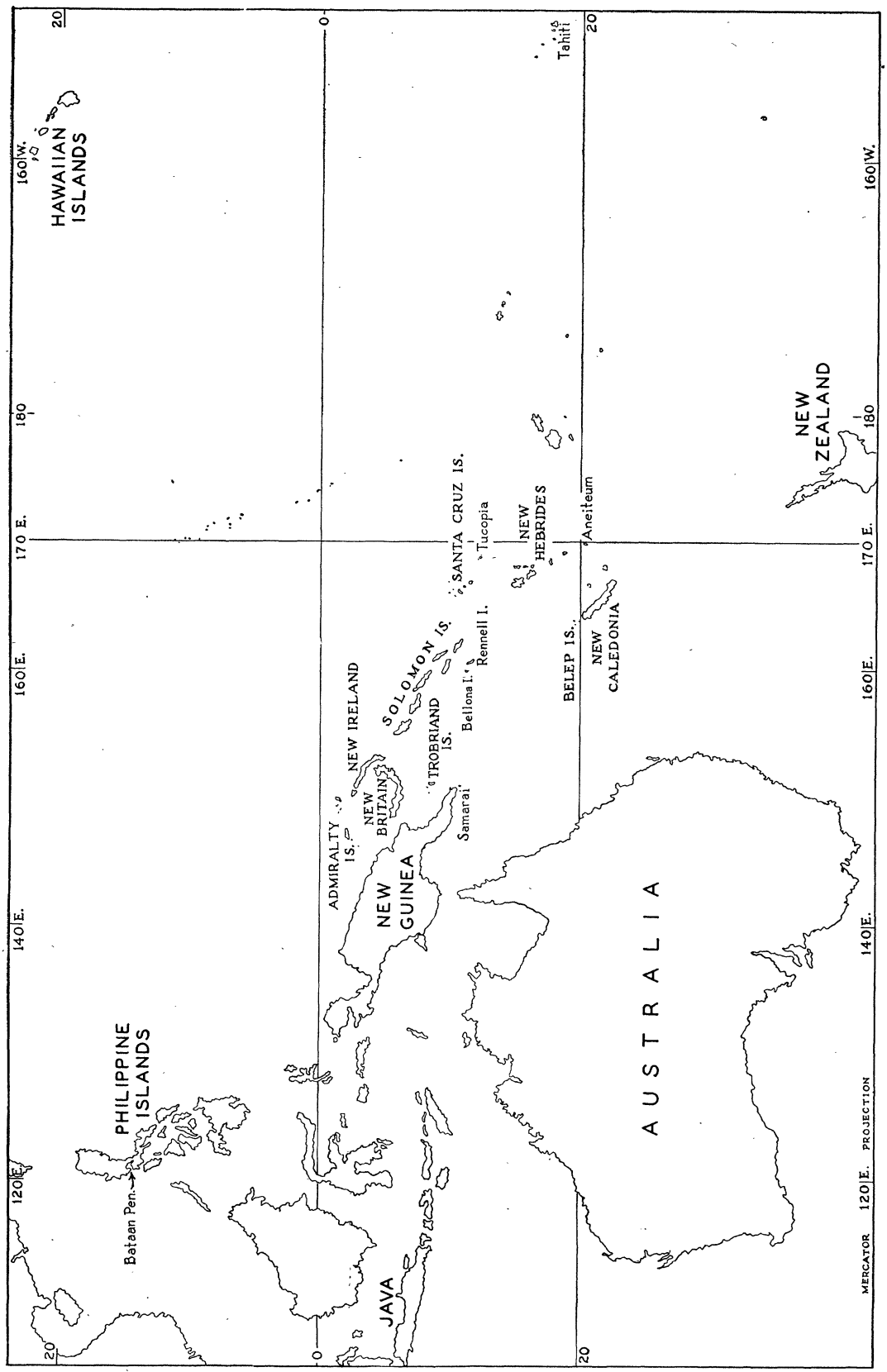
HAWAIIAN ISLANDS
160 W.
20
0
180
170 E.
160 E.
140 E.
120 E.
PHILIPPINE ISLANDS
Bataan Pen.
JAVA
ADMIRALTY IS.
NEW IRELAND
NEW BRITAIN
NEW GUINEA
SOLOMON IS.
TROBRIAND IS.
Samarai
Bellona I.
Rennell I.
SANTA CRUZ IS.
Tucopia
NEW HEBRIDES
BELEP IS.
NEW CALEDONIA
Aneiteum
Tahiti
AUSTRALIA
NEW ZEALAND
MERCATOR 120 E. PROJECTION

FIG. 1.

the distribution of malaria and its carriers, the *Anopheles* mosquitoes, in the Pacific theater of the war.

According to P. A. Buxton, malaria is "believed to occur in all the islands between the equator and 20° S., from New Guinea eastwards to 170° E. The only islands inside this area which are free from malaria are Belep, to the northwest of New Caledonia, and a very few minute islands such as Tucopia. The only malarious island outside that area is Aneityum, which is a fraction of a degree further south than 20° S."[2] In his health surveys of 1930 and 1933, S. M. Lambert failed to find malaria in Rennell and Bellona Islands, but it has since reached Rennell (Lambert, *in lit.*, June 5, 1942), so Buxton's statement is now no doubt substantially correct. Authorities, however, do not agree as to the presence or absence of malaria and *Anopheles* in New Caledonia. M. A. Laveran, in *Comptes Rendus de la Société de Biologie* for 1901 and 1902, A. Leboeuf, in the *Bulletin de la Société de Pathologie Exotique* for 1913, and E. C. Zimmerman, in the *American Naturalist* for May–June, 1942, all specifically comment on the absence of *Anopheles* from New Caledonia. F. W. Edwards, in the "Genera Insectorum," 1932, and F. H. Taylor, in his "Check List of the Culicidae of the Australian Region," 1934, however, both include New Caledonia within the range of *A. punctulatus*. P. A. Buxton, in his review of Taylor's work in the *Tropical Diseases Bulletin* for 1935, does not accept this, and quotes Taylor as subsequently agreeing with him. Fritz Weyer, in "Die Malaria-Übertrager," 1939, however, again records *Anopheles* from New Caledonia. The question is of more than academic interest, as New Caledonia is a vitally strategic island along the supply route between the United States and Australia, and the United States has recently landed troops there.[3] If *Anopheles* are present there, the danger of infection is imminent and the troops will require daily prophylactic doses of such anti-malarials as are available; if they do not exist there, administration of drugs for malaria prophylaxis would be wasteful. In any case, a supply of quinine or a suitable synthetic substitute should be on hand, as *Anopheles* and malaria may be brought in from elsewhere.

The standard works of Edwards and of Taylor, mentioned above, to which the medical entomologist would naturally refer, are misleading in that they fail to give complete lists of the Pacific islands where *Anopheles* are definitely known to occur. Both Edwards and Taylor omit from the range of *Anopheles* the Admiralty and Trobriand Islands, New Britain, New Ireland, the Santa Cruz Islands and Samarai in the China Strait near New Guinea. Weyer omits the Admiralty, Trobriand and Santa Cruz Islands and Samarai. Kumm's paper in the *American Journal of Hygiene Monographic Series,* 1929, is more complete, but his record, now unacceptable, of a third species, the Australian *A. annulipes,* from the New Hebrides, was obtained by reducing *A. farauti* to a synonym of *A. annulipes* instead of *A. punctulatus,* as is now customary. Herms and Gray's record of *A. annulipes* from the New Hebrides, in "Mosquito Control," 1940, is no doubt derived from the same source.

As far as can be ascertained, there are at present in the Pacific Islands east of New Guinea two species and one variety of *Anopheles*. One of the species, *Anopheles punctulatus,* and its variety *molluccensis,* range into the Pacific as far east as the New Hebrides. Both are proven carriers of malaria. The other species, apparently as yet unnamed, is known only from the larvae taken in New Britain.

In view of the fact that an introduced *Anopheles,* carried from Africa by airplane or fast navy destroyer, was responsible for the wide-spread and devastating malaria outbreak in Brazil in 1931, it is important to consider the imminent danger of the spread of other members of the genus in the Pacific region. *Anopheles punctulatus* and its variety *molluccensis* have the most adaptable larvae of all known *Anopheles,* so they may be expected to extend their range beyond the New Hebrides and become established in new localities. According to Swellengrebel and Swellengrebel in the *Bulletin of Entomological Research* for 1920–21, *molluccensis,* wherever it occurs, is very common, breeding everywhere, in all kinds of water, fresh or salt, stagnant or running, dirty or clean. Larvae have been found even in water standing in coconut shells and in native boats. As early as 1928, fear of the introduction of *A. punctulatus* into Tahiti from the New Hebrides was expressed, and the danger of the spread of *Anopheles* through the Pacific islands is, of course, now increased immeasurably as a result of constantly increasing air traffic and disturbed conditions generally.

The islands of Mauritius, Reunion and Barbados long enjoyed immunity from *Anopheles* and malaria, but within the last century all three have suffered severe epidemics. It is not unlikely that New Caledonia, and even Hawaii and the islands of the Central Pacific, will lose their immunity before the end of the present war. As Herms and Gray write, the transport of a fertilized *Anopheles* to the Hawaiian Islands, where malaria is at present almost unknown, might

[2] *Trans. Roy. Soc. Trop. Med and Hyg.*, 19: 420–454, 1925–26. See also P. A. Buxton and G. H. E. Hopkins, "Researches in Polynesia and Melanesia," 3: 51–124, 1927.

[3] The recent outbreak of plague in New Caledonia is referred to elsewhere (E. P. Mumford, "Native Rats and the Plague in the Pacific," *American Scientist,* 30: 212–217, 1942).

ultimately become both a public health and an economic disaster to the Islands. With only a limited supply of quinine or other anti-malarials, the further spread of *Anopheles* and malaria might well affect an entire campaign and even the final outcome of the war in the Pacific.

The problem of mosquito control, which is of the utmost importance, is, of course, beyond the scope of this series of studies on faunal distribution. It has, moreover, been dealt with at length by leading authorities such as Herms and Gray.

As part of this series, revised lists of mosquitoes and other vectors of disease in the Pacific and other islands are being completed for publication in the hope that the dissemination of such information may be of use in the present emergency.

MECHANISM OF ACTION OF ORDINARY WAR GASES

By Professor CHAUNCEY D. LEAKE and DAVID F. MARSH

UNIVERSITY OF CALIFORNIA MEDICAL CENTER, SAN FRANCISCO

CURRENT interest in war gases justifies pharmacological discussion of their mechanism of action. This may help to give a rational background for advice to civilians for reasonably effective protection against, and management of, possible war gas injury.

In general, the intensity of biological action of any chemical is determined by (1) the dosage, in terms of mass of chemical per mass of living material; (2) the ratio of the rate of absorption and distribution of the drug through the living tissue to its rate of excretion or destruction; (3) the physico-chemical properties of the drug, such as its differential solubility in different solvents, its polarity, its molecular configuration and energy organization, its dissociation characteristics and its optical properties, and (4) the peculiarities of the particular type of living tissue involved, such as its age, its metabolic and allergic states and its enzyme balance. These factors may be summarized in short-hand fashion in the following non-mathematical formula:

$$I = (f)\left[D\frac{rA}{rE}\right], \text{ Ch, P.}$$

The concentration (C) of the chemical in the tissues at any given moment after administration is given by the product of D and the ratio of rA to rE.

Consistent appreciation of these factors may aid both in understanding the difference in action of various war gases and also the variation in intensity of effect of the same war gas in the same concentration on different individuals. An appropriate analogy to the latter situation is the difference in response of different people to the same intensity of sunlight or poison ivy.

For this discussion we may limit ourselves to a consideration of the ordinary war gases, such as the lung irritants, like phosgene or chloropicrin, or the vesicants, like mustard gas and lewisite. We may thus disregard such unusual possibilities as catalyzed cyanides or metallic carbonyls, and such gaseous associates of demolition bombs and incendiaries as carbon-monoxide, "nitrous fumes," "blast," hot oil smoke or phosphorus. However, the tissue aggressiveness of "nitrous fumes" suggests that these deserve attention in the same way as ordinary war gases.[1]

As indicated in Table 1, the ordinary war gases may be considered to be chemical relatives of such types of aliphatic hypnotic and inhalation anesthetic agents as alcohol, chloroform and ether. There is general knowledge of the locally irritating powers of these common compounds. Their war gas relatives may owe an increased irritative action to aggressive factors

TABLE 1

CHEMICAL RELATIONS BETWEEN COMMON IRRITANT DRUGS AND TYPICAL WAR GASES

Aliphatic irritant	Corresponding war gas
Alcohol $H–CH_2CH_2–OH$	Ethyl dichloroarsine $H–CH_2CH_2–AsCl_2$
Chloroform $Cl_3C–H$	Chloropicrin $Cl_3C–NO_2$
Ether $(H–CH_2CH_2)_2O$	Mustard gas $(Cl–CH_2CH_2)_2S$

associated with altered halogenation and polarity. These war gases usually contain a rather labile halogen, like chlorine or bromine, which, with the hydrocarbon portion, may be considered to be relatively lipoproteophilic with respect to the rest of the molecule. On the other hand, the war gases also contain more potent polarizing radicles, like oxygen, sulfur, arsenic, a nitro group or oxime, which may be relatively hydrophilic or which may reduce the strength of the halogen bond. Differences in relative water-fat solubilities and in ease of hydrolysis may be important factors in the site of action or in the onset or duration of action, as exemplified in the contrast between lacrimators and vesicants.

One theory explaining the action of war gases is on

[1] Proceedings of a Board of the Chemical Warfare Service appointed for the purpose of investigating conditions incident to the disaster at the Cleveland Hospital Clinic, Cleveland, Ohio, on May 15, 1929. Edgewood Arsenal, Maryland, Lieutenant-Colonel Walter C. Baker, C.W.S., commanding. U. S. Government Printing Office, Washington, 1929, 104 pp.