Public health

Climatic warming and increased malaria incidence in Rwanda

Michael E Loevinsohn

Summary

Global climatic change is expected to increase the incidence of vector-borne diseases, especially malaria. This study assessed the contribution of climate to a malaria epidemic in Rwanda, focusing on the catchment area of one health centre where diagnosis was consistent and non-climatic variables well monitored.

In late 1987 malaria incidence in the area increased by 337% over the 3 previous years. The increase was greatest in groups with little acquired immunity—children under 2 years (564%) and people in high-altitude areas (501%). Case-fatality rose significantly (relative risk=4·85, $p<0·001$). 1987 also saw record high temperatures and rainfall. An autoregressive equation including lagged effects of these two variables explained 80% of the variance in monthly malaria incidence. Temperature (especially mean minimum) predicted incidence best at higher altitudes where malaria had increased most. Empirically derived relations were consistent with the estimated generation time of the disease and with the known sensitivity of the plasmodium parasite to temperature.

The patterns of climatic warming between day and night and among seasons will be critical to the effect on malaria. These findings are most relevant to regions near the altitude or latitude limits of the disease, where several epidemics have lately been reported.

Lancet 1994; **343:** 714–18

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Introduction

Global warming and its associated climatic changes are expected to affect a range of processes related to agricultural production and public health. One of these processes is the transmission of vector-borne diseases, of which malaria is the most widespread, affecting some 270 million people worldwide.[1] An increase in temperatures would allow spread of both anopheline mosquitoes, the vectors of the disease, and plasmodium parasites, the causal agents, to higher latitudes and altitudes. Warming is also expected to increase transmission and prevalence of malaria in areas where it is already established by reducing the interval between the mosquito's blood meals, thus decreasing its generation time, and by shortening sporogony, the incubation period of the parasite in the mosquito.[2,3]

Temperatures in the tropics are expected to increase by 2–3°C at equilibrium in response to a doubling of atmospheric carbon dioxide by the year 2025–2050 unless human activities change substantially.[4] Precipitation in the tropics is predicted to rise, although there are likely to be areas where it will decline. Where changes in rainfall are insufficient to compensate for increased evaporation, mosquito breeding sites will shrink, reducing the impact of warming on malaria. These effects may be modified, however, by human adaptation, including migration and irrigation.

During the past 30 years, the mean temperature in the tropics has risen by about 0·2°C, less than in higher latitudes, but with much spatial variation.[5,6] It is difficult to assess the effect of this change on malaria transmission because of various confounding factors, not least the wide geographical and temporal differences in precipitation and in the effort expended on malaria control. Fragmentary and irregular reporting makes the task even harder in Africa: though it is estimated that 90 million of the world's annual 110 million clinical cases of malaria occur in sub-Saharan Africa, only 2–7 million are reported to WHO.[1] I present evidence here of significant climate-induced increases in malaria incidence within one country and in the catchment areas of individual health centres, where reliable sources of data can more readily be selected.

Methods

Rwanda (1–3°S, 29–31°E) is the most densely populated country in Africa. 95% of the 7·2 million inhabitants live in rural highlands of altitude 1400–2400 m. Rainfall ranges from 800 mm to 1600 mm in a bimodal pattern. Surveys in 1991 near 1400 m in southern Rwanda found that 90% of children aged 2–9 years carried malaria parasites;[7] 90% of infections were due to *Plasmodium falciparum*. Earlier studies in the country identified *Anopheles funestus* and *Anopheles gambiae* (s1) as the dominant vectors.[8]

For Rwanda as a whole, indices of temperature and rainfall were calculated for the period 1961–90. These indices were expressed as departures from long-term means at four weather stations—

Karama (1403 m), Kigali (1495 m), Rubona (1706 m), and Rwerere (2312 m). Trends in malarial incidence were calculated from cases reported by the country's ten prefectures. Although health monitoring is efficient, the reliability of these data is undermined by changes in the number of centres reporting and in case definition. As incidence rose in the late 1980s, many centres based their diagnoses increasingly on clinical signs and symptoms, rather than on microscopic examination of blood smears. This was not the case at the Gikonko Health Centre (GHC), which serves a population of 38 000 in Butare prefecture. Well-staffed and receiving foreign assistance, the centre has since 1975 consistently confirmed clinical suspicion by microscopy. GHC is 10 km from the Rubona weather station. Together, their records provide a valuable data set for examination of the effect of climate on malaria.

Cases (both inpatients and outpatients) were classified by age and "sector" of residence (an administrative unit of 5–10 km² and about 2500 inhabitants). The fourteen sectors in the GHC catchment area were grouped by mean altitude, estimated by sampling along transects drawn on topographic maps. High, mid, and low zones had mean altitudes of 1596 (SD 49) m, 1520 (14) m, and 1485 (19) m, respectively. Incidence was based on population interpolated between census estimates in 1978[9] and 1991.[10]

The relation between climatic variables and monthly malaria incidence was assessed by time series analysis.[11,12] Equations were developed for the catchment area for October, 1975, to December, 1990, and for the three altitude zones for January, 1984, to December, 1989, when reliable records of residence are available. Models were identified after the effects of autocorrelation in the independent variables had been removed by ARIMA procedures, then estimated by the iterative Prais-Winsten generalised least-squares technique. In several cases full maximum likelihood estimates were also calculated, but since there were no substantial differences, only the former results are reported. The choice among model variants consistent with the identified relation was made on the basis of minimum residual error variance and autocorrelation in the residuals. Separate equations were estimated with mean, minimum, and maximum temperatures as independent variables.

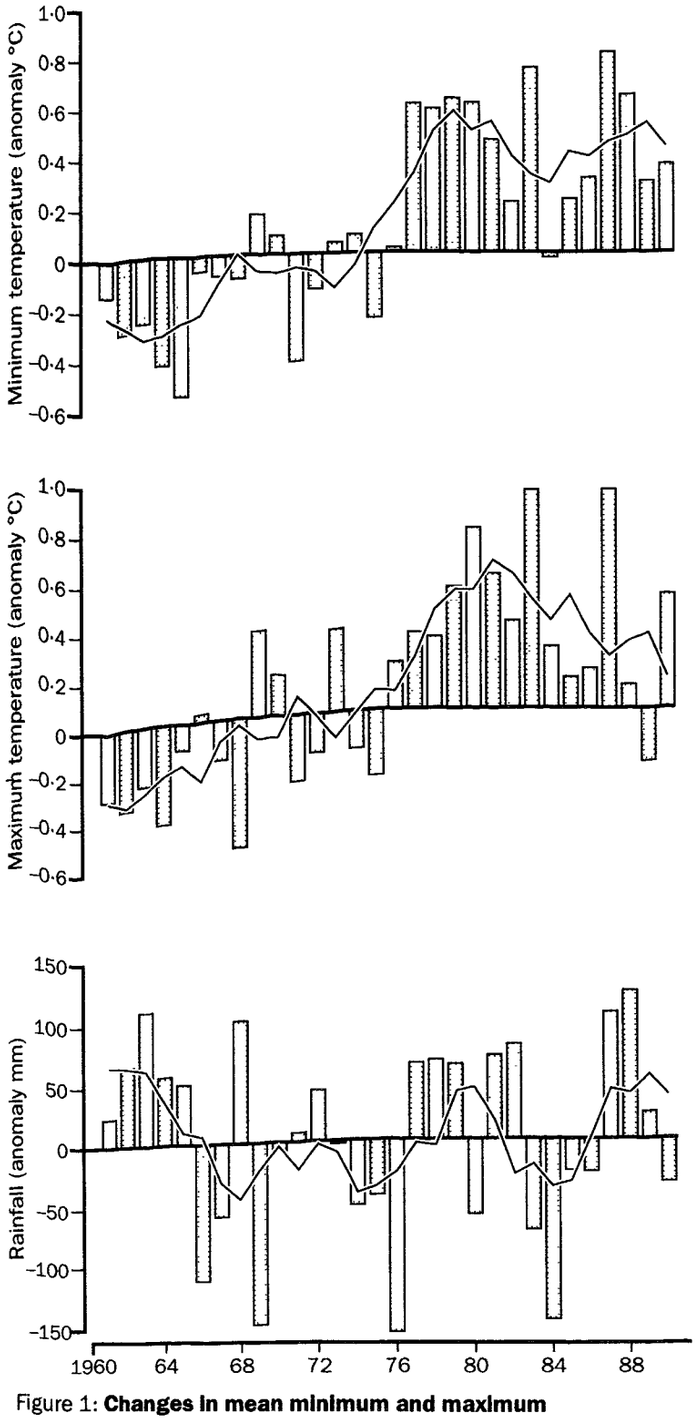

Figure 1: **Changes in mean minimum and maximum temperature and rainfall, expressed as anomalies relative to 1961–80 mean at four weather stations**

Curve is 5-year moving average.

Results

Trends in climate and malaria

Temperature increased greatly in Rwanda between 1961 and 1990 (figure 1). Though maximum (afternoon) temperatures lagged somewhat behind minimum (night-time) temperatures in later years, 1987 was the peak for both, as it was in the tropics as a whole.[6] By contrast with temperature, there was no overall trend in precipitation. Heavy rains in 1987 (the highest since 1930 at Rubona, where records are longest) and 1988, coincided with an especially strong El Niño-Southern Oscillation (ENSO) event. This periodic large-scale air and ocean disturbance is associated with rainfall peaks in equatorial eastern Africa and anomalies elsewhere in the low to mid latitudes.[13]

The late 1980s also saw malaria's establishment in areas where the disease had been rare or absent[14,15] and a steep increase in the incidence nationwide (figure 2). Reported cases rose by 266% between 1984 and 1988, with larger increases in the five prefectures bordering the Nile–Zaire divide (374%) than in the five lower-lying prefectures (240%). The greatest change came in the second half of 1987.

The pattern at GHC was similar (figure 3). The number of malaria cases rose sharply across the catchment area in the second half of 1987 compared with the same period of 1984 (337%). The rise was greater in the high-altitude zone than in the middle and low zones (501 *vs* 323%, $p < 0{\cdot}005$ Mantel-Haenszel). The rate of change did not differ

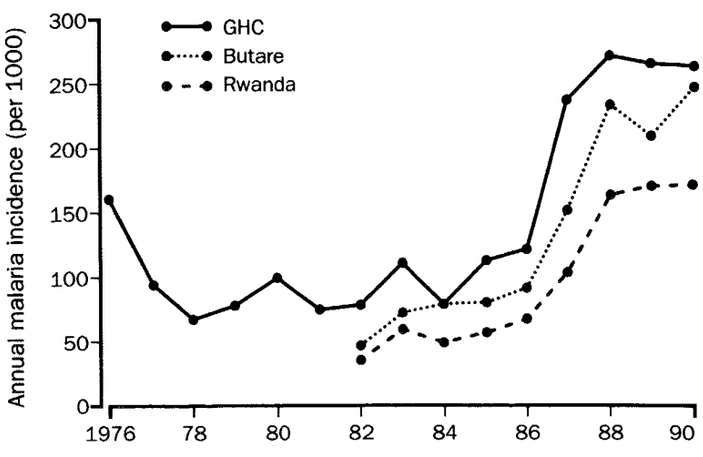

Figure 2: **Changes in malaria incidence at national, provincial, and local levels**

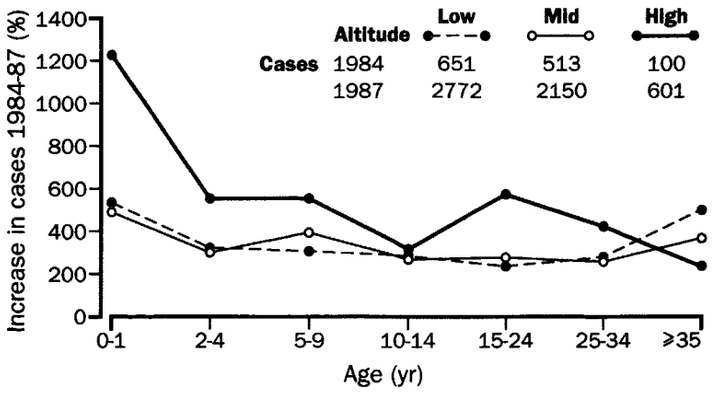

Figure 3: **Percentage increase in malaria cases at GHC between the second halves of 1984 and 1987**

significantly between the mid and low zones. Incidence also increased more in children under 2 years than in older children and adults (564 *vs* 311%; $p < 0.001$). There were no other significant differences in rate of change among the age groups. In the months that followed the peak, malaria declined least among the youngest subjects; compared with the second half of 1987, the number of cases a year later had fallen by 9·7% in children under 2 years but by 22·4% in older groups ($p < 0.005$).

These results are consistent with an intensification in malaria transmission, which increased disease incidence most among individuals with the least acquired immunity, young children and people living at high altitudes where malaria had previously been rare. (Interviews with residents in the highest sector, at above 1700 m, suggest malaria was not endemic there in the early 1980s.) Increased incidence among these susceptible groups led to a rise in serious outcomes. Deaths at GHC in the second half of 1987 exceeded the total for the 3 previous years (15 *vs* 6). The case-fatality rate (among inpatients) rose from 0·5% to 2·5% (relative risk 4·85 [95% CI 1·89–12·4], $p < 0.001$). The acquisition of immunity by survivors probably contributed to the subsequent decline in disease; young children with less developed immune capacities would not have benefited to the same extent.

Climate-malaria relation

Changes in malaria incidence in the catchment area were significantly associated with temperature and rainfall (figure 4). The best-fitting equation for the relation was:

$$\ln I_m = -4{\cdot}32 + 1{\cdot}64 \ln Tn_{m-1} + 0{\cdot}83 \ln Tn_{m-2} + 5{\cdot}34 \times 10^{-4} R_{m-2} + 7{\cdot}7 \times 10^{-4} R_{m-3}$$
$$(0{\cdot}70\text{–}2{\cdot}56) \quad (0{\cdot}12\text{–}1{\cdot}78) \quad (0{\cdot}04\text{–}10{\cdot}3) \quad (2{\cdot}8\text{–}12{\cdot}6)$$

ϱ (autocorrelation coefficient) = 0·89, $R^2 = 0{\cdot}80$; $F_{4,177} = 6{\cdot}60$, $p < 0.001$; where I_m is the incidence in month m, Tn_m the mean minimum temperature, and R_m the rainfall at Rubona. 95% CI for the coefficients are given below the equation. No significant relation was found when mean or maximum temperature replaced the minimum. Climatic variables were significantly related to the logarithm of incidence in all three altitude zones.

Three features of the equation are noteworthy. Firstly, the relation between temperature and malaria incidence is best described as an exponential function with a coefficient greater than 1. In the equations specific for the three altitude zones, this coefficient was 1·90, 3·14, and 3·40; the latter two were significantly greater than 1. These findings suggest pronounced sensitivity to temperature, which accords with what is known of the biology of the malarial parasite and the epidemiology of malaria. The duration of sporogony, the main temperature-dependent step in the parasite's life cycle, decreases hyperbolically with rising temperature near 20°C.[3] The basic reproductive rate of the disease increases exponentially as the duration of sporogony declines, and malaria incidence increases almost linearly with disease reproductive rate, at least until very high values are reached.[16]

Secondly, the equation suggests that temperature and rainfall act on malaria through lags of 1–2 and 2–3 months, respectively. Lags associated with temperature and rainfall in the zone-specific equations were similar. Such delays are consistent with the estimated minimum generation time of a case of *Plasmodium falciparum* malaria[3,17]—40–57 days under prevailing conditions (80% of mean monthly temperatures at Rubona were between 20·2° and 18·7°C during 1976–90). An additional delay for rainfall is the time for runoff and seepage to collect in low-lying breeding sites. Equation 1 suggests that this delay is about 1 month, which is what was found in small catchments under similar

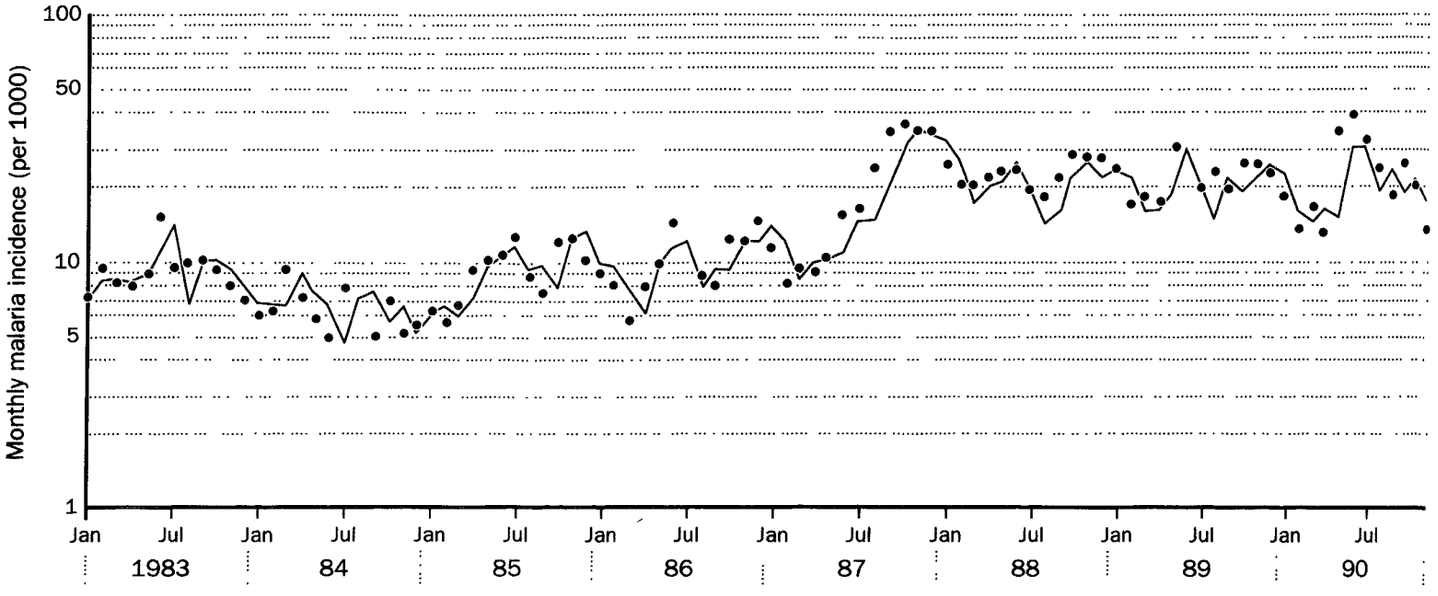

Figure 4: **Monthly malaria incidence in GHC catchment area in relation to climate**
Points = observed values, line = equation 1. Only the last 8 of the 15 years analysed are shown.

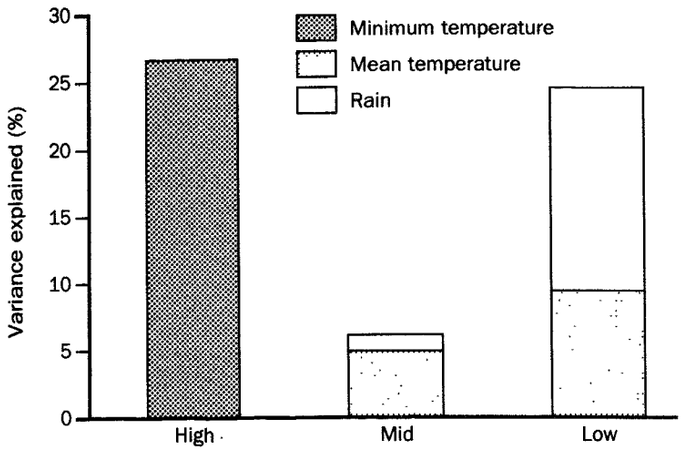

Figure 5: **Proportion of variance of log monthly malaria incidence accounted for by climatic variables in best-fitting equations of three altitude zones**

climatic conditions in nearby Kenya.[12] The effects of rainfall on incidence seemed to be restricted largely to the low altitude zone, which borders broad valleys (figure 5). Rainfall accounted for significant additional variance after temperature had been entered ($p < 0.05$) only in this zone.

Finally, minimum rather than mean temperature was the better predictor of incidence in the catchment area as a whole. This finding would be expected in an area near the altitude limits of malaria's distribution, where extreme temperatures frequently constrain parasite development. The zone-specific equations bear out this interpretation—incidence was most closely related to minimum temperature at higher altitudes and to mean temperature at lower altitudes (figure 5). Temperature explained the change in incidence best in the high-altitude zone, where malaria has increased proportionally most. This finding is again consistent with frequent limitation of transmission by temperature and with the parasite's pronounced sensitivity to temperature at the margins of its range.

Discussion

These findings suggest a link between the upsurge of malaria in Rwanda during the late 1980s and enhanced transmission resulting from the concurrence of increased temperature and rainfall. Non-climatic factors implicated in malaria outbreaks elsewhere[3,18] did not seem to contribute greatly either nationally or in the GHCs catchment area. The role of these factors can be best assessed at GHC level, where documentation is more complete. There was no abrupt suspension of control measures (house spraying ceased in the 1960s)[8] and no large influx of infected or non-immune people by immigration (only 7% of the current population moved into the area between 1980–89, mostly from neighbouring communes where incidence is similar).[19] No major roads or other structures were constructed that might have impeded drainage. Irrigated rice culture expanded slightly during the period but remains concentrated in low-lying areas,[7] where malaria increased least. A famine that might have weakened immunity began in 1989, after malaria incidence had peaked. Parasite resistance to chloroquine (the drug of choice clinically and in self-treatment) did not increase between two studies in the GHC catchment area in late 1986 and 1987, just before and after the rapid rise in malaria incidence.[20] The coherence in the trends from local to national levels (figure 2) suggests a cause or causes acting widely and almost simultaneously, such as changes in weather.

Malaria epidemics occurred during the late 1980s in Botswana, Madagascar, Swaziland, and Zambia. Heavy rains and spreading drug resistance have been proposed in explanation,[1,21] but not rising temperature. All these countries lie near or astride the altitude and latitude limits of malaria and would be vulnerable, as is Rwanda, to the effects of warming. Even small increases in annual mean temperature could have substantial epidemiological effects, depending on how they are distributed. My findings suggest that near the limits of its range, malaria is more sensitive to changes in the minimum than the maximum temperature. There is little other information on the relative changes of these two variables in tropical areas. They may be affected differently by such factors as cloud, wind, and humidity, which are sensitive to global warming.[5]

Also important is the partition of warming among seasons. In the northern hemisphere especially, temperatures have risen more in winter than in other seasons.[6] At Rubona, Rwanda, between 1950 and 1990, minimum temperature increased 70% faster (0·03°C per year) in June–August, the long dry season when nights are coldest, than during the other 9 months. Patterns are similar elsewhere in the region (unpublished). Warming concentrated in the coldest periods may render malaria transmission less seasonal, which would significantly affect incidence.

The empirical relations between climate and malaria presented here will probably not describe the situation in warmer areas, where plasmodium is less sensitive to temperature but where transmission may be exacerbated by greater vector abundance and activity, due especially to more frequent blood meals.[2] My findings suggest, however, that climatic change can have substantial impact in areas near the limits of malaria's distribution and underscore the need to decentralise analysis of these effects. Effective preventive measures, personal and environmental, will be required to mitigate epidemics such as Rwanda has experienced.

I thank the staff of Gikonko Health Centre for making their records available, the Institut des Sciences Agronomiques du Rwanda and Ministère des Transports for climatic data, and Dr T Downing, Dr B Loevinsohn, Dr S Munyantore, and Dr L Sperling, and reviewers at WHO for valuable comments. This study was supported by a grant from the LJS Foundation.

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BOOKSHELF

Brain's diseases of the nervous system

Tenth edition.—*Edited by John Walton. Oxford: Oxford University Press. 1993. Pp 801. £95. ISBN 0-192619691.*

Any book by John Walton offers a welcome feast of information be it on a subject not heretofore crystallised by his remarkable experience, memory, and writing style, or a revision of one of the several textbooks and monographs he writes and edits. This tenth edition of *Brain's diseases of the nervous system* is no exception to the rule. Walton (honoured deservedly in his own country as Lord Walton) originally took over Brain's unfinished text to complete the rewriting of the seventh edition. Editions eight, nine, and this one bear entirely Walton's stamp of clear composition, good editing, comprehensive coverage, and determination to remain up to date. In keeping with that last goal, 19 of the 24 chapters in this new edition represent the contributions of experts within special areas of neurology to supplement Walton's own introductory chapter on basic mechanisms and his sections devoted to nutritional-deficiency disorders, the neurology of general medical disorders, disorders of muscle, and disorders of the autonomic nervous system and thalamus. The overall result admirably meets the challenge faced by an expert-level textbook—it discusses accurately and in some detail what is new in the subject and, at the same time, continues to enunciate fundamental beliefs in the field it represents. What is more, the various chapters generally hang together and suffer from only a minimum of repetition.

The above having been said, there are parts of the book that are especially well done and other parts or approaches that might be reconsidered when the time for composing the eleventh edition rolls around. Charles Warlow's chapter on "Disorders of the cerebral circulation" is the best single short (70 pages) piece on cerebral vascular disease that I have yet encountered. Clearly written, judiciously balanced between scientific information and the art of good medicine, it is a model of what an advanced level textbook ought to contain. Similarly, once one gets accustomed to his propensity for puzzlingly long sentences, Alastair Compston's discussion of neuroimmunology, his descriptions of the biology of multiple sclerosis, and his capacity to relate recent scientific advances to the still incompletely understood pathogenesis of the demyelinating diseases are as clearly informative and up to date as any I have seen. Reflecting a similarly high quality of clarity and substance, David Chadwick weaves together advanced biophysical physiology and the clinical aspects of the epilepsies into an altogether interesting and informative discussion of these often poorly understood disorders. Martin Rosser has lost none of his ability to describe clearly and logically abnormal behavioural states and their mechanisms.

One should also not ignore the high quality of publication. Despite 800 or so pages of text and introductory material the book, although sturdily bound, is handily carried. The printing is clear and the reproductions of brain images, radiographs, photographs, and histological slides are generally done well.

Has the book any faults? Of course, all such textbooks do. Walton's introductory chapter is probably longer than need be and too elemental in scope to be of maximum use to readers of this advanced level volume. Martin Rosser's sections on disorders of higher brain function and cognition are clear and understandable but too short. An ageing population, much head trauma, drugs, and social circumstances all have conspired to increase the incidence and social burdens of the cognitively impaired. Furthermore, the British schools of neuropsychology and quantitative brain imaging have made major contributions to neurological knowledge of human thought and behaviour in recent years. This major textbook surely ought to have a fuller discussion of these advances.

Several topics are given too much attention. Central pontine myelinolysis is discussed three times and illustrated twice. The chapters on spinal cord disorders and rehabilitation partly and unnecessarily repeat each other, even including the same picture twice.

Finally, a word about bibliography. Long lists of references, many of which date back more than a decade, accompany several subsections of almost every chapter and take up considerable space. Many of these citations carry no more than historical interest and some lack even that.