A recent study in the Gambia has shown a strong relationship between risk of death (mainly due to infectious diseases) in young adults and their season of birth (mortality ratio \( MR = 3.7 \) from 14.5 years and \( MR = 10.3 \) from 25 years, \( P < 0.0001 \)). Among several potential causal factors, fetal undernutrition was considered the most plausible. This study is a similar analysis of children and young adults living in rural Senegal, close to the Gambia.

Season of birth was used as a proxy for fetal undernutrition. Indeed, birthweight varies strongly with season in the Gambia, as does women’s weight and pregnancy weight gain. Furthermore, in a randomized trial comparing intervention and control villages, maternal food supplementation increased the birthweight by 201 g in the rainy season (June–October), compared with 94 g in the dry season (November–May).

Since most of these premature deaths were from infections, the authors suggested that maternal malnutrition during the ‘hungry’ season might have deleterious long-lasting effects on the immune status of the fetus. Thus, the ‘fetal origins of disease’ hypothesis, first proposed by Barker and co-authors, may not be limited to chronic (cardiovascular) disease; rather, fetal malnutrition might also ‘programme’ a major risk of infectious disease among adults.

Other factors (malaria, aflatoxin) were also considered by the authors, but were considered less likely causes than undernutrition.

Demographic surveillance conducted by the Institut de Recherche pour le Développement (IRD, formerly named ORSTOM) in a rural area of Senegal since late 1962 offered the
opportunity of examining the relationship between season of birth and risk of early adult death in another West African setting. The geographical proximity of this area to the Gambia, with similar strong seasonal variations in nutritional status and in malaria, makes this comparison particularly interesting.

The objectives of the present report were to provide further evidence for seasonal variation in women’s weight, and to examine the impact of season of birth on the risk of death among children and young adults in this rural Senegalese area.

Population and Methods

Population
The study zone of Niakhar is located in the Sine-Saloum region between the towns of Bambey, Fatick, and Diourbel in central Senegal, 115 km east of the capital city Dakar, and 140 km north of Keneba, the Gambia. It currently comprises 30 villages and about 30 000 residents. The population lives on one food crop (millet) and one cash crop (groundnuts), and field work lasts from May to November (Figure 1). The study area has been described in more detail previously.

Mortality and morbidity
Infant and under-5 mortality rates fell from 223 and 485 per 1000 in the 1960s to 80 and 213 per 1000, respectively, in the 1990s. Both were 3–6 times greater in September–October compared with January–July.

Childhood morbidity and mortality from vaccine-preventable diseases have decreased sharply since the onset of immunization programmes in the 1980s, in particular for measles, pertussis, and neonatal tetanus. However, outbreaks of meningitis and cholera still occur. Young adults also die from maternal mortality (ratio: 516 per 100 000), tuberculosis, and hepatocarcinoma (A Diallo, unpublished observations).

The incidence of disease varies strongly with season. Meningitis, measles, and pertussis peak during the dry season (February–May), while malaria almost exclusively occurs at the end of the rainy season.

The demographic surveillance system
In October 1962, the first demographic survey in the area was launched in eight villages, the ‘Ngayokhem zone’ (≈5000 inhabitants). A continuous follow-up of this population has been maintained ever since. In 1983, 22 additional villages were included in the demographic surveillance to form the ‘Niakhar zone’, including 30 villages.

From 1963 to 1983, censuses were organized at yearly intervals, generally in the dry season (February). However, no census was conducted in 1967, 1975, 1976, or 1979. Demographic surveillance was performed twice yearly from 1983 to 1986, weekly from 1987 to 1997 and at 3-month intervals since March 1997.

At each census, experienced demographic field workers, through visits to all compounds, noted the occurrence and date

Figure 1 Agricultural calendar, rainfall, and mean weight of non-pregnant women by month in the Niakhar area of central Senegal in 1991 (adapted from ref. 5). Cl, clearing; So, sowing; We, weeding; Ha, harvesting
of all births, deaths, marriages, divorces, and out- and immigration which had occurred since the preceding visit. The field workers referred to all residents by name to ensure completeness of new events.\textsuperscript{16}

This surveillance conforms to the Helsinki Declaration and has received approval from the national Senegalese authorities.

Assessment of dates of births

The dates of births which had occurred since the preceding visit were obtained through interviews with mothers using a local calendar of events. Season and specific agricultural activities were important guidelines for this procedure. Systematic registration of pregnancies enabled the monitoring of outcomes, thus facilitating the registration of birth dates.

From 1983 on, the date of registration of birth dates by fieldworkers was also entered into the database. Mean duration between occurrence and registration of births was 3.8 months from 1983 to 1986, 0.3 months from 1987 to 1997, and 2.0 months thereafter.

Cohorts selected for the analysis

Two cohorts with prospective follow-up were selected: the Ngayokhem cohort and the Niakhar cohort. The Ngayokhem cohort consisted of subjects born 1962–2001 in the eight villages followed since 1962 (n = 9192). Among them, 4095 were born prior to 1983. The rate of missing month of birth for this period was 0.9%.

The Niakhar cohort was comprised of the 22,823 children born in the 30 villages 1983–2001. Thus, the 5097 subjects born 1983–2001 in the Ngayokhem zone were included in both cohorts. No subjects had missing information on date of birth.

All subjects born alive and within the study area until March 2001 were included.

Survival analysis

The Cox model was used for survival analysis. The Niakhar cohort was chosen to assess MR by season of birth for infants (0–1 year), 1–5 year olds, and 5–14.5 year old children. The Ngayokhem cohort with the longer follow-up was used to estimate MR from 14.5, 20, and 25 years of age.

Subjects were entered at fixed ages (birth, 1, 5, 14.5, 20, or 25 years) and contributed to the analysis until 31 December 2001, upper limit of age range (when relevant), emigration, or death, whichever came first. Subjects were allowed to re-enter the cohort after migration if they resettled in the area.

Season of birth was defined as in the study by Moore \textit{et al.},\textsuperscript{1} i.e. post-harvest season January–June and hungry season July–December.

Gender was not related to season of birth, and no interaction was found between gender and season of birth in relation to mortality. Gender was therefore excluded from the final analyses. Prior to the use of the Cox model, we tested the proportionality of mortality rates by season of birth for each age interval under study.

Dbase files (Version 4.0) were extracted from the central database and analysed using Epinfo and S+ (version 1995).

Monitoring of nutritional status of women

From 1990 to 1996, nutritional status of women was assessed during vaccination sessions for their infants, organized by IRD in the three dispensaries of the area during the first week of each month.\textsuperscript{17} Women were weighed using a Seca 769 electronic scale precise to the nearest 100 g. Attendance rates were about 80%, each woman attended up to four times (at about 2, 4, 6, and 9 months postpartum) per infant, and the mean number of women per session was 311.

Results

Nutritional status of women

Strong seasonal variations in weight were obvious throughout all 7 years (Figures 1–2). The maximal yearly differences in mean weight were 3.7, 3.0, 3.1, 3.3, 3.5, 3.2, and 3.9 kg, respectively, from 1990 to 1996 ($P < 0.001$ for each year).

Characteristics of study subjects

Main characteristics of subjects born in the Niakhar zone are given in Table 1, for births 1987–1996 (some variables were not collected for earlier and later births). Those born July–December were slightly more likely to be born at home rather than in a dispensary or hospital ($P < 0.001$).

Distribution of month of birth

Seasonal variations in birth rates were apparent with lower than expected proportions in June and July and higher proportions in September and October ($P < 0.001$, Figure 3).

Child survival by season of birth

During infancy the risk of death was slightly but significantly greater for children born July–December (Table 2). No difference was found within the age group 1–5 years, nor 5–14.5 years (Table 2).

Adult survival by season of birth

The MR by season of birth (hungry/post-harvest) from 14.5 years old was 0.77 (95% CI: 0.47, 1.25, Table 3).

From the age of 20 years, the MR for adults born during the hungry season tended to be lower than that of subjects born during the post-harvest season (MR = 0.53), though not significantly below 1 (95% CI: 0.28, 1.02, Table 3). From 25 years of
age, the MR was 0.33, which was not significantly below 1 either (Table 3).

Survival curves by season of birth are shown in Figure 4. Subjects born July–December showed no tendency towards poorer survival during adolescence or adulthood. From 27–37 years, survival seemed less favourable for those born January–June, but at age 37 the survival curves again crossed over (Figure 4).

Distribution of month of birth for the 66 subjects who died after the age of 14.5 years showed no tendency towards more deaths for those born July–December or during any other season (Figure 5).

### Table 1: Main characteristics of newborns by season of birth (Jan–Jun versus Jul–Dec) in the Niakhar zone of rural Senegal (30 villages) 1987–1996

<table>
<thead>
<tr>
<th>Variable</th>
<th>Jan–Jun (n = 5641)</th>
<th>Jul–Dec (n = 6371)</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>2856 (50.6)</td>
<td>3210 (50.4)</td>
<td>0.80</td>
</tr>
<tr>
<td>Girls</td>
<td>2785 (49.4)</td>
<td>3161 (49.6)</td>
<td></td>
</tr>
<tr>
<td>Birth order</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>843 (15.0)</td>
<td>913 (14.3)</td>
<td>0.67</td>
</tr>
<tr>
<td>2–3</td>
<td>1405 (24.9)</td>
<td>1634 (25.7)</td>
<td></td>
</tr>
<tr>
<td>4–6</td>
<td>1790 (31.7)</td>
<td>1999 (31.4)</td>
<td></td>
</tr>
<tr>
<td>&gt;6</td>
<td>1600 (28.4)</td>
<td>1817 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Place of birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>4745 (84.9)</td>
<td>5518 (87.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dispensary</td>
<td>724 (12.9)</td>
<td>711 (11.3)</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>122 (2.2)</td>
<td>89 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Village</td>
<td>1502 (26.6)</td>
<td>1719 (27.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>Hamlet</td>
<td>4139 (73.4)</td>
<td>4652 (73.0)</td>
<td></td>
</tr>
<tr>
<td>Residents in compound</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>737 (13.1)</td>
<td>822 (12.9)</td>
<td>0.96</td>
</tr>
<tr>
<td>10–19</td>
<td>1996 (35.4)</td>
<td>2261 (35.5)</td>
<td></td>
</tr>
<tr>
<td>&gt;20</td>
<td>2908 (51.6)</td>
<td>3288 (51.6)</td>
<td></td>
</tr>
<tr>
<td>Maternal schooling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>5187 (92.5)</td>
<td>5807 (91.8)</td>
<td>0.10</td>
</tr>
<tr>
<td>Primary</td>
<td>367 (6.5)</td>
<td>469 (7.4)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>52 (0.9)</td>
<td>47 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Maternal activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outside the home</td>
<td>643 (12.1)</td>
<td>752 (12.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>Home only</td>
<td>4638 (87.9)</td>
<td>5344 (87.7)</td>
<td></td>
</tr>
<tr>
<td>Maternal fieldwork</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4910 (92.8)</td>
<td>5651 (92.9)</td>
<td>0.84</td>
</tr>
<tr>
<td>No</td>
<td>381 (7.2)</td>
<td>431 (7.1)</td>
<td></td>
</tr>
</tbody>
</table>


### Table 2: Mortality ratios (MR) by season of birth (Jul–Dec/Jan–June) in the Niakhar zone of rural Senegal (30 villages, followed 1983–2001)

<table>
<thead>
<tr>
<th>Season</th>
<th>Lost to follow-up</th>
<th>Follow-up (person-years)</th>
<th>Mean follow-up (years)</th>
<th>MR 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1 year old</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan–June</td>
<td>828</td>
<td>305</td>
<td>10 428</td>
<td>9580</td>
<td>0.9</td>
</tr>
<tr>
<td>Jul–Dec</td>
<td>1103</td>
<td>391</td>
<td>12 050</td>
<td>10 671</td>
<td>0.9</td>
</tr>
<tr>
<td>1–5 years old</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan–June</td>
<td>1074</td>
<td>573</td>
<td>8691</td>
<td>27 528</td>
<td>3.2</td>
</tr>
<tr>
<td>Jul–Dec</td>
<td>1169</td>
<td>642</td>
<td>9974</td>
<td>30 170</td>
<td>3.0</td>
</tr>
<tr>
<td>5–14.5 years old</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan–June</td>
<td>171</td>
<td>503</td>
<td>5345</td>
<td>31 059</td>
<td>5.8</td>
</tr>
<tr>
<td>Jul–Dec</td>
<td>197</td>
<td>561</td>
<td>6041</td>
<td>33 568</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Discussion

No significant difference in the risk of death among young adults was observed in relation to season of birth in rural Senegal, despite large seasonal variations in women’s weight. The difference in mean weight varied from 3.0–3.9 kg from 1990–1996 compared with 2–4 kg in the Gambia, and the timing of seasonal variations was the same.

During the first year of life only, Senegalese children born in the hungry season had a higher risk of death. However, the difference was moderate (MR = 1.18), and due to the close relationship between season of birth, season of death, and age at death (which is closely related to risk of death during infancy), the relative effects of prenatal and postnatal season on mortality cannot be differentiated for infants. In the Keneba area, infants born February–April and particularly May–July also had lower risks of death.

One limitation of our study was the fact that duration of follow-up for adults was shorter than in the study by Moore et al., i.e. up to 39 years compared with 48 in the Gambia. However, the relative risk of death associated with birth in the hungry season in the Keneba area was so high (more than tenfold from 25 years old) that if a similar tendency indeed existed in Senegal, it would have been detected even with a shorter follow-up.

The statistical power for detecting an increased mortality risk among births in the hungry season from 14.5 years old was
The quality of date of birth is critical, since lack of specificity and misclassification would bias results towards similarity of risk between groups. The cohorts were defined with this in mind by selecting only subjects with prospective assessment of dates of birth. From 1962 to 1983, when demographic visits were performed less frequently, the rate of missing month of birth was very small (<1%). The date-of-births were estimated by interviews with the mothers using calendars of local events. Therefore, for 1962–1983 the estimation would have a precision of ±1 month. However, misclassification of season of birth, as defined here, is probably insignificant and cannot explain the absence of a relationship of mortality risk with season of birth.

Considering the completeness of death registration, data are highly reliable, except for infants born 1962–1982. Indeed, infants who are born and die between two censuses may be omitted by their families when censuses are conducted at yearly intervals or less. Furthermore, a bias related to season of birth cannot be ruled out, since censuses were usually conducted at the beginning of the post-harvest season (in February), so that infants born in the post-harvest season who later died were perhaps more likely to be omitted. However, the MR for infancy was computed for the period 1983–2001 when follow-up visits were conducted at 6-month intervals or less, and was unchanged when computed only for subjects born 1987–2001 (MR = 1.18, 95% CI: 1.06, 1.31, P = 0.002). For the Ngayokhem cohort of subjects born 1962–2001, the MR was slightly greater (MR = 1.23, 95% CI: 1.09, 1.39; P = 0.001).

Our inability to replicate the Gambian results could have several different explanations. First, season of birth may be related to risk of death only in the Gambia. Indeed, a prospective population follow-up from 1978 to 2000 in peri-urban Bissau, Guinea-Bissau, 22 160 km south of Keneba, found a lower risk of death among subjects born during the hungry season. Prospective follow-up of 1457 children born 1972–2000 conducted at annual or bi-annual intervals from 1978 to 2000, yielded 23 deaths (excluding 3 deaths due to bombs) during 5249 person-years. Cox’s survival analysis provided an MR by season of birth, from 15 years old, of 0.36 (95% CI: 0.13, 0.99). Adjusting for gender provided a MR of 0.37 (95% CI: 0.13, 1.04).

Limitations to these data were that subjects were, at most, 22 years old at the end of follow-up, that the study area was peri-urban, presumably with less seasonal variation in nutritional status than in agricultural societies; and that for those born 1972–1977 birth dates were determined retrospectively in 1978, using a local seasonal calendar. The better

The eight villages of the Ngayokhem zone are included in the 30 villages of the Niakhar zone (see Table 2).
survival of Guineans born during the hungry season may have occurred by chance, especially since the age range (15–22 years) was different from that during which Senegalese adults, born in the hungry season, tended to die less frequently (27–37 years).

A second possibility is that the phenomenon responsible for differences in survival in the Gambia was present in Senegal in the 1940s and 1950s as well, but had disappeared prior to 1962. Unfortunately, Senegalese adults born in the 1950s could not be included in the present analysis because their birth dates, collected by the recall method in 1962, were not considered precise.

Finally, this phenomenon may no longer exist in the Gambia. Indeed, a recent study revealed no evidence of immunodeficiency in 6–10 year old children born July–December in the Keneba area. Thus, the increasing MR with increasing age in the Gambia would be a cohort effect (i.e. the relationship exists only in older generations) rather than an age effect. In this case, fetal undernutrition cannot be the causal factor. Indeed, strong seasonal variations in nutritional status were still present in the 1980s (maternal weight) and in the 1990s (birthweight).

Which other causal factors could be considered? Moore et al. discussed maternal malaria during pregnancy, fetal, or postnatal exposure to aflatoxin (peak in April–May) and postnatal exposure to gastrointestinal rotavirus infection (epidemics in January), but argued that the timing of these seasonal factors did not correlate well with that of high-risk births. Conversely, the timings of maternal weight loss (May–October/November) and of lower than average birthweights (June–December) are very similar and closely mimic the pattern of death by season of birth. Hence, birthweight is mainly affected by maternal undernutrition during the last months of fetal life, and thus, this could thus also be the case for immunocompetence.

The results of our study support the hypothesis that malaria and aflatoxin do not explain the Gambian finding. Indeed, malaria is intensely transmitted from September to November in Niakhar, and exposure to aflatoxin is common in the Sine-Saloum region during the dry season. With regard to rotavirus infection, a peak in the prevalence of diarrhoea in January–February has also been described for infants in Niakhar, and rotavirus infection in infants in Guinea-Bissau, south of Senegal, occurs almost exclusively from January to March.

In conclusion, longitudinally collected data on birth and death over a long period of time are rare in developing countries. The prospectively collected Senegalese data presented here do not replicate the Gambian finding of an increased adult mortality risk for subjects born during the hungry season, strongly suggesting that their poor survival is not explained by either maternal undernutrition, malaria, or aflatoxin exposure.

Acknowledgements

The long-lasting, dedicated efforts of field workers, supervisors and data managers, in conjunction with the positive attitude and patient collaboration of the population, made this study possible. Pierre Cantrelle, Michel Garenne, Anouch Chahnazarian and Valérie Delaunay directed the demographic surveillance of the Niakhar study zone during parts of the study period. Ernest Faye, who participated in demographic surveillance from 1967 to 2001 (since 1989 as the head of the field station in Niakhar), provided extensive information on the demographic surveillance system. Sophie Moore and Jacques Vaugelade gave helpful comments on an earlier version of the manuscript. The European Community, the World Health Organization, the Task Force for Child Survival, Aventis-Pasteur and the IRD (formerly named ORSTOM) provided financial support to research projects conducted in the Niakhar study zone. This paper is dedicated to Anouch Chahnazarian who died in 1993.

KEY MESSAGES

- A recent analysis showed that young Gambians born during the ‘hungry’ season had a highly increased risk of death, mainly from infections. The authors suggested that undernutrition in pregnant women induces delayed immunodeficiency in the fetus.
- In the present study, no excess risk of death was found for young adults born in the hungry season in Senegal, a neighbouring country to the Gambia, despite seasonal maternal undernutrition.
- Fetal undernutrition is not a plausible explanation for the observed increased risk of death among young Gambians born in the hungry season.

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‘Sereer women winnowing groundnuts’, author: Eric Bénéfice