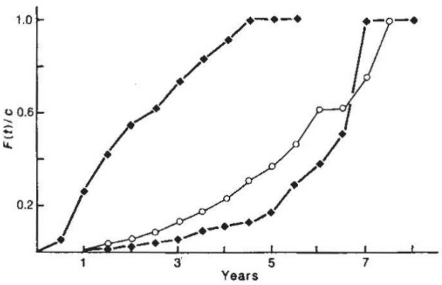

Nonparametric estimates of $F(t)$, the probability that the incubation time is less than t for children (◆, top curve), adults (o) and elderly patients (◆, bottom curve). The unspecified constant c is the probability that the incubation time is less than 7.5 years. Note that c cannot be estimated from the transfusion data alone, and that different values of c could apply to the separate age groups.

it is necessary to obtain an external estimate of c.

Medley *et al.* comment that estimates of incubation time characteristics such as means and medians are based on extrapolation, and this is true. In fact the difficulties are even more severe. Because of the identifiability problems, even low percentiles of the incubation distribution cannot be estimated without additional assumptions. With parametric assumptions, such as those used by Medley *et al.*, identifiability problems still persist. Thus although point estimates of median incubation times can be obtained, the confidence intervals associated with those estimates are very broad. Under a Weibull model for $f(s)$ and an exponential model for $h(x)$, point estimates (with 95 % confidence intervals) of the median incubation times in years are 2.0 (1.4, 4.0), 7.3 (4.6, ∞), and 5.8 (4.3, ∞) for the young, middle, and elderly age groups, respectively. (Here, ∞ indicates a large but finite upper terminus.) So, not much faith can be placed in the point estimates obtained. Similar remarks apply to the estimation of the total number of infected individuals.

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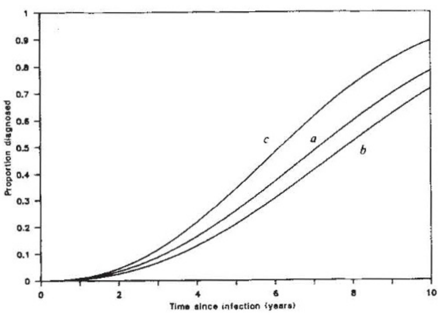
MEDLEY *ET AL.* REPLY — Kalbfleisch and Lawless are correct in their assertion that if the probability distribution of the incubation period of AIDS is truncated at some time point T (all observations beyond the present time, T, are unobserved), then only the conditional distribution up to T can be estimated without parametric assumption concerning the form of the full distribution of incubation periods. For the matters of concern to epidemiologists and public-health planners, namely understanding and prediction of observed trends, the conditional distribution is of rather little interest and hence parametric formulation is inevitable. We emphasized the obvious hazards of this approach by showing explicitly the different estimates arising from two plausible parametric assumptions (the Weibull and gamma distributions)[1]. We agree that the point estimates of median and mean incubation periods have large errors, and that these are best assessed by likelihood ratio arguments.

In our previous papers[1,2] we noted the importance of updating estimates of the distribution of the incubation period as more data become available. The Centers for Disease Control (CDC) in Atlanta provided a recent data set covering reports of AIDS cases received up to 8 February 1988. In these data there are 560 cases with certain dates of transfusion (infection), diagnosis and report, compared with 297 in the previous data. We have so far considered only those cases who were older than 12 years at diagnosis (512 cases).

In this preliminary analysis we have adopted the same approach as before [1,2]. We assume parametric forms for the distributed incubation period and the distributed reporting lag, and an exponential increase in the incidence of infective transfusions up to early 1985 when routine screening of donated blood was introduced in the United States. We assume that the infection rate has been constant since then. CDC estimate that even after the introduction of screening, about 400 infective donations per year are tested during the period before antibodies against HIV are produced, and therefore appear negative (M. Morgan, personal communication). We are able to discriminate between different parametric forms for the incubation period by comparison of the independent assessment of the rate of infective transfusions with that



Comparison of the cumulative distributions (Weibull) for the incubation period of AIDS in transfusion-associated patients estimated from: A, all adults (>12 yr) notified to CDC by 8 February 1988; b, people older than 4 yr and less than 60 yr; and c, all cases, regardless of age. Estimates b and c are from a data set in which people were diagnosed before July 1986 and notified to CDC by January 1987. Exact comparisons are not possible because of the difference in age groupings between the two data sets. The most notable features are the similarity of shape between the distributions, and the fact that the means and medians are similar between a and b and between a and c after 2 yr further observation.

estimated from the data.

We have considered the Weibull and gamma distributions as possible candidates for the incubation-period distribution. The estimated means (medians) are 7.59 yr (7.32 yr) and 24.07 yr (20.84 yr), respectively, and, as previously, the log-likelihood values do not allow a distinction to be made between the distributions. The estimated annual rates of infective transfusion since the introduction of screening, however, are 333 and 2,161, respectively, which leads us to reject the gamma distribution in favour of the Weibull as a descritption of the data.

Also of interest is the observation that the estimate of the overall mean for the adult age classes is similar to that reported in previous publications [1,2]. It is difficult to make direct comparisons as the format of the data has altered. The similarity of the estimates may suggest that the estimate is approaching the true mean of the full distribution, however. Past estimates of this mean have tended to increase with the length of the observation period of transfusion-associated AIDS cases [1-3].

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Fish farming and aquaculture

SIR—The article "Fish farming and influenza pandemics" by Christoph Scholtissek and Ernest Naylor (*Nature* **331**, 215; 1988) has been widely reported in Asian and Western newspapers. We feel that it deserves clarification because of adverse effects it might have on the promotion of aquaculture in developing countries.

The authors claim that widespread development of integrated farming systems involving pigs, poultry and fish could lead to the creation of influenza A viruses with new surface antigens against which the human population does not possess specific neutralizing antibodies. The article suggests that pigs may be "mixing vessels" where normally separate avian and human influenza virus reservoirs meet, and where genetic reassortment takes place between them, giving rise to new human pandemic influenza strains.

We share the authors' concern that the

promotion of integrated farming systems in developing countries to alleviate malnutrition should not create potential health hazards. However, we believe that the inferred link between fish farming development in the Third World and human influenza pandemics is grossly overstated.

Pigs and poultry have been brought together without fish on traditional mixed farms in Asia and Europe for centuries, although more recent trends in livestock development in both East and West are towards monocultures because of management and marketing considerations. Most integrated livestock–fish farms raise a single species of terrestrial animal with fish. In the examples cited by the authors, only 16 per cent of the freshwater fish farms in Hong Kong with livestock have more than one species of livestock. Similarly pig–hen–fish culture is not widespread in Thailand and the example discussed in the Commentary (hens in cages above pigs which consume hen faeces) is based on a single farm which has since discontinued the practice in favour of pig–fish integration (the original article implied, but did not actually state, that the practice is widespread — another example of the danger in making a generalization from a very limited data base).

Poultry manure has little nutritional value for intensively fed monogastric animals such as pigs because most of the nitrogen is in a non-proteinaceous form. In short, the co-location of pigs and poultry to supply manure for fish culture is neither prevalent nor likely to become so.

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NAYLOR AND SCHOLTISSEK REPLY — In Pullin and Shehadeh (1980), cited in our article, M.N. Delmendo (Food and Agriculture Organization, Bangkok) states "Thailand practices integrated poultry–pig–fish farming, particularly in the central plain where the water supply is abundant". We claimed no more than that pig–poultry–fish systems do occur and pointed out a potential health hazard of expanding the practice of co-locating pigs and poultry around fish ponds, both points which Edwards *et al.* appear to concede.

It would be encouraging if pig–fish systems could be kept separate from poultry–fish systems but to achieve that seems likely to require qualification of a published proposal submitted in February 1988 to the Consultative Group on International Agricultural Research (CGIAR). The proposal being considered by CGIAR argues forcefully for "fully integrated crop/livestock/fish farming with maximal efficiency of use of on-farm resources" and emphasizes the need for a "whole farm" approach to the development of tropical freshwater aquaculture.

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Massless particles from a perfect fluid

SIR—Your report[1] on the experiments of Danzmann, Meyerhoff *et al.*[2] on heavy-ion collisions encourages me to draw attention (even if hesitatingly) to a phenomenon which Basilis Xanthopoulos and I[3-5] have encountered in the context of the collision of plane impulsive gravitational waves in general relativity.

Briefly, the phenomenon is this: a perfect fluid, in which the energy-density (ε) equals the pressure (p) and the velocity of sound equals the velocity of light, can be transformed into massless particles, or 'null dust'. More precisely, we showed that the presence of an ($\varepsilon = p$)-fluid in the region of the space-time, after the instant of collision of two impulsive gravitational waves, implies that it is the result of a transformation of null dust following the leading edge of the impulsive waves. This transformation, first encountered in the framework of general relativity, is, as Roger Penrose pointed out to us, equally possible in the framework of special relativity (see ref. 6 and ref. 5 Fig. 1). There can be no doubt that the transformation described does and will take place under the circumstances considered. Indeed, as we wrote, "If the reality of this ultimate state of matter i.e. a fluid with $\varepsilon = p$ is accepted, then the fact that such matter can be converted into null dust, both in the frameworks of general and special relativity, gives credence to the possibility that null dust, as classically defined, may have an equal reality." The principal question concerns the reality of an ($\varepsilon = p$)-fluid.

It was pointed out by Zel'dovich[6] in 1962 that the ultimate equation of state of electrically neutral matter consisting of charged constituents of opposite signs, is one in which equality between the energy-density and the pressure is attained and the velocity of sound equals the velocity of light. (For a simple account of Zel'dovich's arguments see ref. 7.) Zel'dovich estimates that the density at which the ultimate equation of state may be attained is 3×10^{16} g cm^{-3}, that is, ~100 times the nuclear density, 3×10^{14} g cm^{-3}. However, already at densities of 3×10^{15} g cm^{-3}, we may expect $p\sim\frac{1}{3}\varepsilon$—the conventional limiting form of the equation of state for a fully relativistic gas.

If we accept the attainability of the equation of state $p = \varepsilon$ as reasonable, how is the null dust described, in the context in which it is transformed into an ($\varepsilon = p$)-fluid? In the framework of general relativity, the Ricci tensor, R^{ij}, is related to the energy-momentum tensor, T^{ij}, by Einstein's equation

$$R^{ij} = -2(T^{ij} - \tfrac{1}{2}g^{lm}T_{lm}g^{ij})$$

with the conventional relativistic units. For an ($\varepsilon = p$)-fluid this relation gives

$$R^{ij} = -4\varepsilon u^i u^j,$$

where u^i denotes the time-like four-velocity of the fluid. Null dust is now described by the relation

$$R^{ij} = \text{constant } k^i k^j$$

where k^i is a null vector. In other words, an ($\varepsilon - p$)-fluid becomes null dust when $u^i \to k^i$, as it does at the shock fronts.

We now turn to the possible relevance of the foregoing remarks to the experiments on the heavy-ion (uranium–thorium) collisions. If we describe the collision as being between two fluids with a density $\rho\sim3\times10^{14}$ g cm^{-3}, then we may expect that at the instant of collision a reflected shock wave results. It is known that the compression following such a reflection can be quite high if the effective 'ratio of specific heats' γ is close to 1. Thus the compression can be as high as 23 even for $\gamma = 1.2$. Because $\gamma\to1$ even at densities as 'low' as 3×10^{15} g cm^{-3}, it would not appear unreasonable to suppose that a compression exceeding 50 is possible under the conditions of the experiments and that a state of matter approaching Zel'dovich's ultimate state occurs. And if it does, why should we not suppose that conversion to null dust, having the characteristics we have described, takes place?

It does not seem likely that the phenomenon described is relevant to the experiments of Danzmann *et al.*[2] because in their experiments, the energy of the collisions was so arranged that the nuclei just grazed one another. But it may be relevant to experiments of more energetic collisions (apparently now being planned) in which the nuclei will strike one another with such strength that a shock wave of the kind described may indeed result, with the attendant phenomena.

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