THE TABLE. *Comparison of PCR with smear test.*

	Leprosy type[a]		
	L	B	T
PCR(+)/smear(+)	8/8	2/2	0/0
PCR(+)/smear(−)	40/60	3/3	4/7
Total	68	5	7

[a] L = Lepromatus; B = borderline; T = tuberculoid leprosy.

of the annealing temperature was essential to prevent nonspecific amplification with human genomic DNA. The accuracy of the temperature setting varies with each PCR processor, and unstable experimental conditions are thought to be likely in developing countries because of variations in electrical voltage and current, which may influence the temperature setting of the processor. Therefore, primers for PCR with higher specificity are desirable for screening tests conducted in the field. Because of the enormous sensitivity of PCR compared with conventional acid-fast staining, *M. leprae* were even detected from tuberculoid leprosy patients. Although most previous studies used skin-biopsy tissue as the DNA source, our results confirmed the suitability of smear-examination needles for leprosy screening by PCR. The need for further treatment in treated PCR-positive patients will vary from case to case, but positivity in untreated patients means that treatment is necessary in all cases. Using such needles, PCR can become a powerful tool for leprosy screening in endemic regions, allowing treatment to be started at an early stage.

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Genetic Vaccines Against Genetically Infective Macromolecules?

TO THE EDITOR:

On 27 September 1991 a report was published in *The Guardian* newspaper [News and Notes, Lepr. Rev. 63 (1992) 94–95] telling how Professor Lex van der Ploeg and Dr. Mary Gwo-Shu Lee are inserting genes into parasites, thus producing parasites which, while perfectly healthy and living in the laboratory, are doomed to die after only a day or two in their human host. What, one might ask, is the relevance of this work—clearly of considerable interest to lay readers—to Hansen's disease? With Hansen's bacilli exactly the opposite applies; that is, they appear to be perfectly healthy and replicating in some human hosts some of the time, but are always "doomed to die" after variable periods—usually of a few days—in the laboratory.

Failure to address seriously the problem of the refusal of Hansen's bacilli to behave like other cultivable mycobacteria is not new. In 1964, I pointed out ([1]) that the statement that *Mycobacterium leprae* could not be cultivated *in vitro* ([7]) was a great advance on the usual idea that *in vitro* cultivation had hitherto been unsuccessful, implying that if only we could obtain the correct physiochemical conditions this technical procedure would become possible. For this, I was perhaps understandably taken to task

and told that my implication that the human leprosy bacillus would never be cultured was inconsistent with a part of published work carried out at the National Institute for Medical Research, London, where *for the previous 10 years* researchers had been studying the tissue-culture conditions and *conditions in cell-free media* for the cultivation and growth of both rat and *human leprosy bacilli* ([8]) (my italics).

It is clearly dangerous to use the word "never" as applied to scientific investigations and experiments, but many distinguished investigators have been trying to cultivate Hansen's bacilli *in vitro* for a very long time. If the work referred to is still continuing, I calculate that to date this represents 38 years of unsuccessful endeavor in one research institute alone. Perhaps this is at least partly because a redefinition of parasitology as suggested by Lumsden ([6]) is required, especially as it applies to the study of the taxonomy of Hansen's bacilli ([3]). It is difficult to understand why this requirement does not seem to have been met when computer simulation of molecular events occurring *in vitro* are so well advanced, and when a start is being made in dissecting the complex conditions *in vivo* of host factors in the production of microbial virulence determinant ([9]).

The above-mentioned report from *The Guardian* has an all too familiar ring about it. In 1981 in *The Lancet,* Stoner, *et al.* ([10]) stated that leprosy was designated a chronic mycobacterial infection with polar forms and a complex of intermediate presentations. The causative organism, *Mycobacterium leprae,* was remarkable for its nontoxicity and its adaptation to growth in the peripheral nerves of the human host. Nowhere in this paper was the *in vitro* noncultivability of Hansen's bacillus (*M. leprae*) mentioned. *In the same issue of The Lancet,* Emery ([4]) reported that the very few DNA experiments carried out at that time required containment in excess of category II. Biological containment was achieved by using microorganisms which had been so attenuated (crippled) that they could not survive *except* in laboratory culture conditions (my italics).

It is to be hoped that the communication gap between the disciplines of theoretical molecular biology and clinical hansenology is beginning to narrow. If not, I predict—despite success in a related field in which plasmid-coated microprojectiles were employed ([11])—delay in the production and testing of genetic vaccines against leprosy. This delay is likely until it is more widely appreciated that such vaccines need to be directed against self-replicating, genetic infective agents in the human subcutaneous axoplasmic nexus and the pigment-bearing layer of the skin laterally transmitted to them ([12]) by naturally genetically infected nonreplicating (carrier) mycobacteria in the *micro*environments in which molecular damage progresses ([2]) (my italics).

If the practical difficulties of field use of genetic vaccines prove to be insurmountable, chemotherapy of invaded axons is an option which cannot be excluded ([5]).

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