encouragement and advice. This work was supported by the Spastics Society and by an anonymous gift.

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Received April 16; accepted May 7, 1975.

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Why didn't Gregor Mendel find linkage?

IT is quite often said that Mendel was very fortunate not to run into the complication of linkage during his experiments. He used seven genes and the pea has only seven chromosomes. Some have said that had he taken just one more, he would have had problems. This, however, is a gross oversimplification. The actual situation, most probably, is shown in Table 1. This shows that Mendel worked with three genes in chromosome 4, two genes in chromosome 1, and one gene in each of chromosome 5 and 7. It seems at first glance that, out of the 21 dihybrid combinations Mendel theoretically could have studied, no less than four (that is, *a–i*, *v–fa*, *v–le*, *fa–le*) ought to have resulted in linkages. As found, however, in hundreds of crosses and shown by the genetic map of the pea[1], *a* and *i* in chromosome 1 are so distantly located on the chromosome that no linkage is normally detected. The same is true for *v* or *le* on the one hand, and *fa* on the other, in chromosome 4. This leaves *v–le*, which ought to have shown linkage.

Mendel, however, seems not to have published this particular combination and thus, presumably, never made the appropriate cross to obtain both genes segregating simultaneously. It is therefore not so astonishing that Mendel did not run into the complication of linkage, although he did not avoid it by choosing one gene from each chromosome.

Table 1 Relationship between modern genetic terminology and character pairs used by Mendel

Character pair used by Mendel	Alleles in modern terminology	Located in chromosome
Seed colour, yellow–green	*I–i*	1
Seed coat and flowers, coloured–white	*A–a*	1
Mature pods, smooth expanded–wrinkled indented	*V–v*	4
Inflorescences, from leaf axils–umbellate in top of plant	*Fa–fa*	4
Plant height, >1m–around 0.5 m	*Le–le*	4
Unripe pods, green–yellow	*Gp–gp*	5
Mature seeds, smooth–wrinkled	*R–r*	7

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Received March 5; accepted June 4, 1975.

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Defect of macrophage function in the antibody response to sheep erythrocytes in systemic *Mycobacterium lepraemurium* infection

THE need for macrophages for optimal antibody responses, both *in vivo* and *in vitro*, to certain antigens is now established[1,2] and this paper describes experiments which have used this requirement to demonstrate a deficiency of macrophage function in mice experimentally infected with the rodent leprosy bacillus, *Mycobacterium lepraemurium*. This organism is an obligate intracellular dweller and is found particularly inside cells of the macrophage series although in terminal infection other cell types may be invaded. Systemically infected mice characteristically show macrophages overloaded with bacilli, ever increasing numbers of granulomata and increasing spleno- and hepatomegaly[3]. There is an increase in the phagocytic activity of the spleen and liver at an early stage of infection (I.N.B. and V.S.Š., in preparation) indicative of alterations in macrophage function and we report here experiments which show that the *in vivo* and *in vitro* antibody response to sheep erythrocytes (SRBC) is depressed at later stages of infection. The results indicate a defect of macrophage function.

Young adult CBA female mice were injected intravenously with 10^9 *M. lepraemurium* freshly isolated from the heavily infected livers of mice infected 4–6 months previously (I.N.B. and H. N. Krenzien, in preparation). At 11–15 weeks after infection, when the present experiments were carried out, the mice appeared clinically healthy but at autopsy showed gross enlargement of liver and spleen. Ziehl-Neelsen stain revealed the presence of numerous mycobacteria in macrophages of various tissues, particularly liver, spleen and bone marrow. Uninfected mice of the same age and sex were used as controls. The *in vivo* antibody response was measured in mice injected intravenously with either 5×10^6 or 10^9 SRBC. Four days later, the number of antibody producing cells (PFC) present in the spleen of each mouse was determined using the method of Cunningham[4]. The *in vitro* response of spleen cells cultured for 4 d according to the method of Marbrook[5] was measured in the same way.

The results given in Table 1 show that the antibody response *in vivo* was reduced 11 weeks after infection and even more so at 14 weeks. This depression was more pronounced in animals injected with the smaller number of SRBC. It seemed greater when the results were expressed as PFC per 10 spleen cells because there was a 4–5-fold increase in the cellularity of the spleens from infected compared with normal mice. Serum antibody levels were also reduced in infected mice (results not shown). Spleen cells from infected animals cultured *in vitro* in the presence of SRBC failed to generate the expected number of PFC, particularly at 14 weeks.