Most previous work on synovial cells in tissue culture involved trypsinization, a procedure which would select against establishment of macrophage cultures. The method used in the present study was similar to that described by Lackington (1959). 76 cultures containing 20 per cent. heat-inactivated serum (from a single human pool), 50 per cent. whole synovial fluid, and 30 per cent. Eagle's medium were set up in Leighton tubes. Of 61 successful cultures, 47 were from patients with rheumatoid arthritis, twelve from patients with other inflammatory articular disease, and two from cases of primary generalized osteoarthritis.

The majority of the cells resembled those seen in cultures of peripheral blood from healthy donors. Multinucleate cells were present in varying numbers. All synovial cultures also contained large pale cells with abundant cytoplasm. 28 synovial cultures showed massive syncytial formations similar to those described by Palmer (1969).

Eight cultures grown on araldite and sandwich-embedded were examined by electron microscopy. This confirmed that a cell type, deficient in lysosomes and distinct from the characteristic macrophage, was present in synovial cultures. The nature of this cell has not yet been established.

References

- LACKINGTON, C. (1959) *Arthr. and Rheum.*, 2, 42 (Tissue culture of fibroblasts and round cells from arthritic synovial fluid).
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Discussion

DR. A. J. PALFREY (*London*) Dr. Glen Bott for the last 3 years has been studying material from rabbit knee joints at St. Thomas's Hospital. She uses a trypsinization technique followed by culture and has studied both the washings and the cultures by electron microscopy. She has also studied the synovial membrane of the normal joint after this lavage technique and has shown that some of the surface cells of the synovial membrane have indeed disappeared as a result of that technique. The cells which she gets in culture, allowing for differences of electron microscopy technique, seem to me to be remarkably similar to those you are describing. She too has been plagued by crystalline-like structures, very similar in appearance to yours, which she attributed to the medium. As early as 4 hours after the start of the culture a large pale cell appeared with very few organelles. I wondered whether you had seen a comparable cell?

DR. MACKAY No. I think that the main feature of these cultures on electron microscopy is a cell which looks very much like a macrophage with its filopodia, but with a complete absence of lysosomes. These are large pale cells and appear very early in the life of the culture. In fact, as soon as the cells have spread, it is possible to distinguish them. I am very interested to hear about this work.

PROF. E. G. L. BYWATERS (*London*) When you examine synovial membrane from rheumatoid patients after synovectomy, you sometimes see that the whole of the surface is formed of columnar-type cells with very many multinucleate cells, rather like those you have shown.

My impression is that these are from knees which have been relatively fixed before surgery and have not had the opportunity of moving and perhaps disintegrating the surface by movement. Do you think that the multinucleate cells you have shown are related at all to either the A or the B type cells that have been described?

DR. MACKAY This is a very difficult question to answer because, in saying we believe this is like the reticular macrophage which Dr. Stuart has described, we have also to take into account the behaviour in terms of dye-uptake in culture. It would be very difficult to distinguish the cell in its situation *in vivo*.

Uptake of ^{14}C -Thymidine by Lymphocyte Cultures exposed to Human Synovial Fluid. By M. JEAN DAVEY (*Rheumatic Diseases Unit, Northern General Hospital, Edinburgh*)

Synovial fluids from thirteen patients with rheumatoid arthritis were tested as possible sources of antigen from altered tissues or infecting micro-organisms. Lymphocytes were separated from human blood by centrifugation through a Triosil-Ficoll mixture and microcultures were set up. The uptake of ^{14}C -thymidine was used as a measure of lymphocyte transformation.

In an autologous system, seven out of thirteen fluids caused slight to marked lymphocyte transformation at 6 days. Eleven of the thirteen synovial fluids were tested against autologous cells in the presence of phytohaemagglutinin (PHA) and nine of these caused enhancement of the PHA-induced response. Eleven synovial fluids were tested against homologous lymphocytes from rheumatoid patients: four of these caused slight transformation and five enhanced the lymphocyte response to PHA. In experiments with homologous lymphocytes from non-rheumatoid donors, four out of eleven synovial fluids caused a slight increase of ^{14}C -thymidine uptake, while six out of twelve enhanced the PHA response.

The increased uptake of ^{14}C -thymidine in lymphocyte cultures containing synovial fluid could have been due to:

- (1) Stimulation by an antigen to which the lymphocytes were sensitive;
- (2) Stimulation by anti-lymphocyte antibody;
- (3) Stimulation by lymphocyte mitogenic factor or other lymphokines;
- (4) Uptake of thymidine by micro-organisms replicating in the cultures;
- (5) Improvement of the lymphocyte culture conditions.

Discussion

DR. D. M. WEIR (*Edinburgh*) Regarding the possibility of this effect's being due to mitogenic factor, or to antibody, as you suggest, it should be feasible to test for this by fractionating the joint fluid on Sephadex G 200. You could separate out the MIF because it moves with the albumin fraction and the antibody would come out in one of the other fractions. Have you tried this?

DR. DAVEY Yes. We have carried out preliminary experiments using both Sephadex and DEAE fractionation, but we have had negative results so far.

DR. D. RAJAPAKSE (London) In one set of experiments the harvesting was done on the 5th day and in the other on the 6th day. Might this not account for wide variation in the uptake of thymidine?

DR. DAVEY In the first group of experiments we did not find any marked difference in the results, whether cultures were harvested at day 5 or day 6, but this is clearly very late in lymphocyte culture time and there tended to be a fairly wide variation. It is late even for antigen stimulation, and I think that in some of the cultures the pH had dropped so much that we were getting rather slight effects.

Review of the Results of Excision of the Metatarsal Heads in Patients with Rheumatoid Arthritis. By D. K. FAITHFUL and D. L. SAVILL (*Princess Margaret Rose Hospital, Edinburgh*)

The results of excision of the metatarsal heads on account of pain in the forefoot in 77 patients with rheumatoid arthritis are reviewed. There were 62 females and fifteen males in the group. Ages ranged from 23 to 74 years. Follow-up ranged from 2 months to 5 years (average 2.2 years). Complications included the development of haematomata requiring release in three feet, wound infection in seven, and delayed wound closure in seven. The results of surgery were assessed in three grades:

- I. Unlimited, pain-free walking in normal shoes.
- II. Some residual pain on walking requiring the wearing of insoles in normal shoes.
- III. Persistent pain on walking not relieved by conservative measures and requiring further surgery.

Of 147 feet operated on, 118 were classed as Grade I, fourteen as Grade II, and fifteen as Grade III.

Of the fourteen in Grade II, eight had persistent pain as a result of pressure on a metatarsal remnant, four had discomfort attributed to wound infection, one had persistent hallux rigidus on one side, and in one the cause of pain was not obvious.

In the fifteen in Grade III, the poor results were attributed to irregular resection of the metatarsals in nine, inappropriate operation in three, and no obvious cause in three.

The fact that in 80 per cent. of feet operated on symptoms were abolished and the wearing of normal shoes made possible makes this procedure one of the most reliable in the treatment of rheumatoid arthritis.

Discussion

DR. A. G. S. HILL (Stoke Mandeville) What is the average length of stay in hospital for these patients?

MR. FAITHFUL It is usually about 4 weeks. After 3 weeks they start walking and by the end of the fourth week they are confident in their sandals and they go home.

DR. A. G. S. HILL (Stoke Mandeville) This always seems to be rather disappointing in the sense that this very productive operation involves a rather disproportionate length of stay in hospital, during which very little is happening because the patient isn't weight bearing.

DR. D. A. PITKEATHLY (Manchester) Have you any experience of treating psoriatic arthropathy with this same operation? In my experience it has been less successful.

MR. FAITHFUL There was one case in which the patient developed hallux rigidus on both sides. We feel that these patients should probably have a Keller's operation, with removal of the base of the first proximal phalanx as well. This patient in fact had this done and there was a good result with relief of pain.

DR. A. G. S. HILL (Stoke Mandeville) Could we ask Dr. Pitkeathly why the result was disappointing in his psoriatic patients?

DR. D. A. PITKEATHLY (Manchester) My feeling is that the metatarsal heads were so irregular, so jagged, to begin with that perhaps the surgeon had more difficulty in trimming them properly, but this was only my impression.

DR. A. G. S. HILL (Stoke Mandeville) Did you refuse any patients for operation because you thought the vascularity was poor?

MR. FAITHFUL Not that I am aware of, no.

PROF. E. G. L. BYWATERS (London) How did you test for this?

MR. FAITHFUL Mainly by testing the pulses and also by seeing the return of circulation in the toes preoperatively. I know Mr. Kessel likes to carry out an arteriogram on his patients before he operates on them, but we did not think this was necessary.

DR. J. A. D. ANDERSON (London) I am interested in this 4-week period in bed, because in my department we are studying progressive patient care, trying to get people out of expensive beds into less costly ones. Would you like to suggest how long these people have to be in the most expensive (Class I) type of bed?

MR. FAITHFUL It has been the policy of this unit to keep them in bed for 3 weeks. We have found that if we get them up on crutches before that, or try to get them home, their feet tend to swell. It is quite a big operation on the forefoot and any swelling might interfere with the blood supply to the foot. For this reason we like to have them in bed with their feet up in the air.

DR. MAUREEN ASHWORTH (Stoke Mandeville) We have found that if we use a dorsal incision the patient needs to spend only 3 weeks in hospital for both feet to be done. Without the plantar incision they are more rapidly mobile and the callosities heal spontaneously.

MR. FAITHFUL Yes, I believe this was the operation described by Mr. Fowler. He also removed a segment of skin from the sole as well, but you don't remove the skin? And you find that the weight-bearing area is not affected on the sole? One of the main reasons for using the plantar incision is to remove this segment of skin: we feel this