The presence of resistance to polyoma tumour isografts in adult rats pre-treated with the virus might be due to the induction by the virus of the same antigen in the cells it infects. These antigenic transformation leads to the rejection of these cells in the adult and immunological competent animal whereas in new-born rats these cells may go further proliferating and eventually give rise to a tumour[3]. There remains, however, to explain why rats injected at birth and tested when adult may show a slight but significant resistance to polyoma tumour isografts. When they do not develop polyoma tumours, one may speculate that the cells infected by the virus, and thereby antigenically transformed, pre-immunized the animal but did not acquire a neoplastic character or were rejected afterwards. When they do develop polyoma tumours and yet are found resistant to the isografts, it becomes difficult to understand why these animals do not reject their own tumours. Although highly speculative, one could, however, consider the hypothesis that rats injected with polyoma virus at birth do not reject neoplastic transformed cells, being immunologically non-reactive, but do not either become tolerant for these cells. At the time their immunological system is built up, in most instances the polyoma tumour cells could be too numerous to be rejected but could pre-immunize the animal sufficiently to enable it to reject a very small inoculum of transplanted isologous polyoma tumour cells.

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A Glycosidase Abnormality in Synovial Membrane in Joint Disease

Polysaccharide–protein complexes are known or suspected to undergo depolymerization or incomplete polymerization in rheumatoid arthritis[1], osteoarthritis[2] and intervertebral disk prolapse[3].

We have, therefore, investigated in synovial membrane the activity of enzymes participating in the degradation of oligosaccharides derived from hyaluronic acid[4], and have found an apparent relationship between β-*N*-acetylglucosaminidase activity, and what can be termed clinically the 'reactivity' of various disease processes.

Specimens of synovial membrane were removed at operation from the knee joints of patients suffering from four clinically distinguishable conditions, namely, internal derangements in the acute and in the quiescent state, osteoarthritis, and rheumatoid arthritis.

No true 'normals' can be quoted, as autopsy material was considered not comparable, but it is thought that the group of interval menisectomies—that is, those in whom a torn semi-lunar cartilage was being removed as an elective procedure without any recent trauma—must approximate closely to normal. In order to limit the number of variables involved, all patients were in the age group 25–45 years: senile osteoarthritis is therefore not included, and the group of 'degenerations' comprises those joints in which there was some predisposing cause, such as an old fracture or internal derangement, accompanied by visible fibrillation or actual loss of articular cartilage.

The specimens for assay, identified by serial number only, were placed in dry sterile containers and immediately refrigerated at 4° C. They were then homogenized and assayed for β-*N*-acetylglucosaminidase activity using ρ-nitrophenyl-β-*N*-acetylglucosamine as the substrate[5].

Table 1. β-*N*-Acetylglucosaminidase activity in 35 consecutive specimen. of synovial membrane in four different abnormalities of the knee-joints The results are expressed as micrograms of ρ-nitrophenyl liberated per hour per gram of tissue (wet weight) at 37° C; and are arranged in descending order of activity

No.	Interval menisectomy	Menisectomy with naked-eye hyperæmia of the synovium	Degeneration of meniscus or of articular cartilage	Rheumatoid arthritis
1				36,300
2				30,500
3				28,370
4				26,450
5				25,520
6				18,910
7				17,020
8				16,040
9				14,000
10			13,890	
11				13,720
12				12,470
13			12,420	
14			11,600	
15		9,970		
16				9,200
17		8,820		
18				8,090
19			7,690	
20				7,020
21		6,770		
22			6,370	
23		5,120		
24			5,010	
25			4,870	
26		3,990		
27				4,300
28		3,986		
29				3,350
30	2,900			
31	2,540			
32	2,160			
33	1,880			
34	1,330			
35				1,060

Thirty-five consecutive specimens gave the results shown in Table 1. No detailed analysis can be undertaken on the basis of this number of estimations, but the general pattern is clear. β-*N*-Acetylglucosaminidase has never been shown to be other than a catabolizing enzyme; and the figures, therefore, confirm that breakdown of tissue is increased in all three abnormalities above, and suggest that the turnover of polysaccharide is much accelerated, both in the so-called degenerative conditions and in rheumatoid arthritis. The wide scatter of results in this last group is puzzling, and may perhaps be associated with cyclical activity of the disease. High enzyme activity tended to be associated with clinical acuteness, as judged on the heat, swelling, and tenderness of the affected joints. There was no apparent correlation with Rose Waaler titre.

The possible relationship of this abnormal enzyme activity to the ætiology of the various processes is interesting, particularly in rheumatoid arthritis, where the enzyme activity is so markedly increased, and where already, on general grounds, there is evidence that enzyme-determined factors are important[6].

The synthesis of 2-acetamido-2-deoxy-gluconolactone, a highly-specific, non-toxic inhibitor of β-*N*-acetylglucosaminidase[5], provides a possible theoretical method of restoring the enzymological balance and perhaps affecting the disease process. However, the clinical results of administration of this enzyme inhibitor to patients with rheumatoid arthritis and allied diseases have so far been unreliable.

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