

Number, size, and distribution of Peyer's patches in the human small intestine

Part I The development of Peyer's patches

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EDITORIAL SYNOPSIS The presence of Peyer's patches is commonly taken for granted but this is the first serious study of the incidence and development of Peyer's patches before and after birth.

The number of Peyer's patches found in the various parts of the human small intestine has never been accurately determined. Most textbooks of anatomy put their number at 20 to 30 (Gray 1962), and only slight variations of these figures are given from one textbook to another. However, Sappey (1877), Passow (1885), and Gundobin (1892) occasionally found 70 or more patches, and Hellmann (1921) in his studies on status thymico-lymphaticus found as many as 246 patches in young children who had died suddenly and unexpectedly from a wide variety of causes.

The present study was undertaken to find out how many patches there are in the normal human gut and to investigate what happens to them before and after birth.

CASES STUDIED

Specimens of small intestine were obtained from 14 necropsies on premature infants who were either stillborn or died shortly after birth, and from 24 necropsies on full-term infants and children up to the age of 14 years. The investigations were limited to necropsies carried out within a few hours of death, and to patients with no clinical history or pathological evidence of disease referable to the gastrointestinal tract or reticulo-endothelial system.

METHODS OF INVESTIGATION

The specimens were opened along their mesenteric borders and washed in running water for at least 24 hours until the washing fluid was free of mucus, blood, and food residues. Large Peyer's patches were then easily seen and their number recorded. The duodenum,

jejunum, and ileum were measured, the jejunum being defined as the proximal two-fifths of the small intestine between the duodeno-jejunal flexure and the ileocaecal valve.

The specimens were next placed in dilute acetic acid for 24 hours to fix the nuclei. Because Peyer's patches consist almost entirely of nuclear material the fixed patches stand out clearly as white opaque superficial plaques against a semitranslucent greyish background.

The follicular content of the patches was made more apparent by staining with 0.5% polychrome methylene blue for one minute after washing the fixed specimens in water. They were rinsed freely to remove excess stain, and left to stand in water for one hour before examination to permit good differentiation between the Peyer's patches and the surrounding tissues. The dark bluish-black patches then contrasted with the lighter bluish-green of the rest of the specimen (Figs. 1 and 2). If the contrast was not sharp further treatment with dilute acetic acid followed by washing in running water for 10 minutes produced a satisfactory result.

The number of follicles inside a patch were counted with the help of a dissecting microscope, using transillumination and 8.75 × magnification (Fig. 3). Only those patches containing more than five follicles were counted. Separate records were kept of patches containing more than 25 follicles, and patches measuring more than 4 cm. in length.

Finally, blocks were taken for histology from patches in the duodenum, distal jejunum, and terminal ileum. These were fixed in formol saline, and paraffin sections were stained with haematoxylin and eosin to show cellular detail, and impregnated with silver salts to demonstrate reticulin. Initially these sections were made to confirm that the patches were in fact collections of lymphoid follicles. Because the histological detail was found to be remarkably preserved in the majority of sections examined they were later used to study the

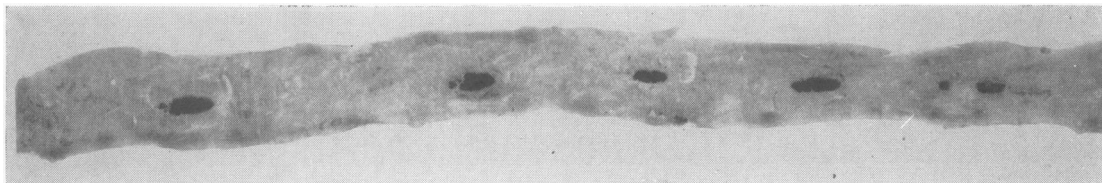


FIG. 1. *Peyer's patches in distal jejunum of case 22. Methylene blue staining and transillumination ($\times 0.9$).*



FIG. 2. *Peyer's patches in terminal ileum of case 22. Methylene blue staining and transillumination ($\times 2.0$).*

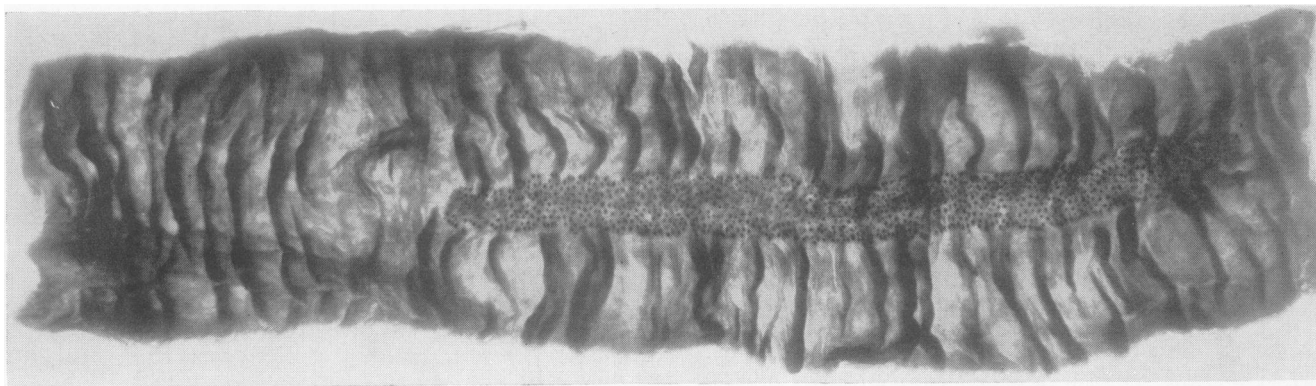


FIG. 3. *Peyer's patch in proximal ileum, showing follicular structure of case 37. Methylene blue staining and transillumination ($\times 1.0$).*

microscopic anatomy and the follicular content of the patches.

The only difficulty experienced with these methods of investigation was in the gross differentiation of Brunner's glands from Peyer's patches. Peyer's patches stained darkly, were well localized, sharply defined, and had smooth, round edges. Brunner's glands, however, stained

lightly, were diffuse, poorly defined, and had blurred edges.

RESULTS

NUMBER The number of Peyer's patches found in 14 specimens from premature infants are given in

Table I. The number of patches found in 24 specimens from full-term infants and children are given in Table II. Mean values for selected age groups are given in Table III. It will be seen that the number of patches varied from 45 at 24 weeks' gestation to 305 at 12 years, with mean values varying from 59 before 30 weeks' gestation to 239 at puberty.

The tables show that there are considerable numbers of both large and small Peyer's patches in the human gastrointestinal tract, and that they are well developed early on in foetal life. Although there is considerable individual variation there is a general tendency for the patches to increase in size and number with increasing age. The number of patches

found, therefore, bears some relationship to age, body weight, and the length of the small intestine.

SHAPE The Peyer's patches were generally oval or rectangular in shape and situated on the anti-mesenteric border. In the duodenum and terminal ileum, and occasionally in the proximal jejunum, the patches were situated at random around the gut wall. A few bizarrely shaped patches were invariably found in the proximal jejunum and around the ileo-caecal valve. These patches were sometimes serpigenous in outline, and several had small side branches two or three follicles wide.

TABLE I

NUMBER OF PEYER'S PATCHES FOUND DURING THE PERIOD OF GESTATION

Case No.	Period of Gestation (weeks)	Sex	Body Weight (kg.)	Length of Small Intestine (cm.)	No. of Patches with More than Five Follicles				Total No. of Patches with More than 25 Follicles
					Duodenum	Jejunum	Ileum	Total	
1	24	F	0.8	148	0	8	37	45	—
2	28	M	1.7	192	0	33	30	63	33
3	28	F	1.0	192	0	15	48	63	41
4	29	M	1.2	142	0	19	46	65	33
5	29	M	1.3	208	1	21	44	66	30
6	29	M	1.9	147	1	17	35	53	33
7	30	F	1.3	189	0	35	62	97	50
8	31	F	1.3	247	0	17	48	65	37
9	32	M	1.4	119	0	12	41	53	29
10	34	M	1.1	118	0	19	39	58	21
11	34	M	2.2	242	0	22	51	73	42
12	34	F	1.6	182	0	22	57	79	52
13	36	F	3.4	230	0	46	50	96	54
14	37	M	1.7	205	0	25	73	98	51

TABLE II

NUMBER OF PEYER'S PATCHES FOUND IN INFANCY AND CHILDHOOD

Case No.	Age	Sex	Body Weight (kg.)	Length of Small Intestine (cm.)	No. of Patches with More than Five Follicles				Total No. of Patches with More than 25 Follicles
					Duodenum	Jejunum	Ileum	Total	
15	0	F	4.5	397	2	50	71	123	59
16	0	F	4.0	420	4	48	63	115	73
17	0	F	2.7	288	0	39	39	78	41
18	0	F	2.3	278	0	43	57	100	58
19	0	F	2.0	211	2	30	64	96	46
20	0	M	2.8	287	0	23	81	104	53
21	6 days	M	2.6	165	0	33	42	75	33
22	8 wk.	M	2.6	332	0	31	68	99	67
23	8 wk.	F	4.2	481	0	50	80	130	86
24	9 wk.	M	3.1	470	0	43	37	80	50
25	7 mth.	F	7.7	505	5	66	103	174	68
26	9 mth.	M	12	439	4	57	123	184	79
27	12 mth.	M	6.6	427	4	39	80	123	54
28	16 mth.	M	15	560	22	84	62	168	76
29	20 mth.	F	11	428	3	49	70	122	52
30	35 mth.	M	—	558	2	129	113	244	106
31	48 mth.	F	16	431	15	66	57	138	67
32	56 mth.	F	35	534	6	49	70	122	50
33	72 mth.	M	30	548	4	54	103	161	72
34	12 yr.	F	33	761	5	58	59	122	50
35	12 yr.	F	45	622	11	99	148	258	95
36	12 yr.	M	39	805	11	118	176	305	126
37	13 yr.	F	50	695	10	116	136	262	118
38	14 yr.	M	58	707	4	93	152	249	125

TABLE III

MEAN VALUE OF NUMBER AND SIZE OF PEYER'S PATCHES FOUND IN SELECTED AGE GROUPS

Age Group	No. of Cases	Mean Body Weight (kg.)	Mean Length of Small Intestine (cm.)	Mean No. of Patches	
				With More than Five Follicles	With More than 25 Follicles
<i>Before term</i>					
24-29 weeks	6	1.3	172	59	34
30-39 weeks	8	1.7	192	79	42
<i>After term</i>					
0-10 weeks	10	3.1	333	100	57
3-12 months	3	8.7	457	160	67
13-72 months	6	21	510	161	71
12-14 years	5	45	718	239	103

SIZE AND DISTRIBUTION Duodenal patches were present in only five of the first 25 specimens examined. After 9 weeks of age small patches were invariably found below the ampulla of Vater. In only two cases (26 and 38) were patches found between the pylorus and the ampulla.

Although the ileum usually contained larger and more numerous patches than the jejunum this was not always the case. Five specimens (cases 2, 24, 28, 30, 31) contained smaller but more numerous patches in the jejunum than in the ileum. Bearing in mind that the jejunum is only two-thirds the length of the ileum a further nine specimens (cases 13, 15, 16, 17, 18, 21, 32, 34, 37) contained smaller but relatively more numerous patches in the jejunum than in the ileum.

No patch measuring more than 4 cm. in length was found in specimens from premature infants. After term one or two such patches were found in the distal jejunum of six specimens, and a variable number were found in the ileum of 18 specimens. Although the patches with the largest surface area were situated close to the ileocaecal valve the longest patches were usually found in the proximal ileum. The longest patch, found in the proximal ileum of case 37, measured 9.9 cm. in length.

FOLLICULAR PATTERN Studies of the follicular content of the Peyer's patches showed that their increasing size was related to an increase in the number of follicles present. The larger the patch the greater was the number of follicles found within it. Microscopy showed that the patches were only one follicle thick, the follicles being intimately related to the overlying epithelium. Occasionally thick patches were found in the terminal ileum of well-nourished infants and young children and gross examination suggested that these patches were two or three follicles thick. Sections taken for histology, however, showed a papillary appearance similar to that shown in Figure 4. These patches were still only one follicle thick, and the intimate relationship between the

individual follicle and the overlying epithelium was preserved.

DISCUSSION

The methods used in this study are relatively crude and give only a rough idea of how much lymphoid tissue is actually present in the human small intestine. It is clear, however, that there are more Peyer's patches than is generally recognized, and certainly more than the figures usually quoted in textbooks of anatomy.

FOLLICULAR CONTENT According to Ziegler (1850) the number of follicles in a patch varies from 20 to 400. Gundobin (1892) counted 30 to 70 follicles in the smaller patches and found the number in the larger patches too difficult to evaluate. In the present study the longest patch contained over 980 follicles (Fig. 3). The smallest patches generally contained 10 to 20 follicles, the medium size patches 60 to 120 follicles, and the larger ones 180 to 260 follicles.



FIG. 4. Histology of Peyer's patch in terminal ileum, showing papillary pattern. Haematoxylin and eosin ($\times 5$).

DEVELOPMENT Due to lack of suitable fresh material it was not possible to examine any specimen before the 24th week of foetal life when 45 well-defined Peyer's patches were found. Lymphopoiesis is, however, found in the wall of the small intestine as early as the 15th week of foetal life (Eberl-Rothe and Langegger, 1953), and Peyer's patches are said to be well developed by the end of the fourth and the beginning of the fifth month of gestation (Baginsky, 1882; Cho, 1931).

Animal investigations have tended to suggest that the general pattern of lymphoid tissue in the intestine is laid down early in foetal life. Removal of Peyer's patches after birth, for example, is not followed by compensatory new formation of lymphoid tissue at other sites (Sanders and Florey, 1940), but by hypertrophy and hyperplasia of the existing lymphoid tissue (Kelsall and Crabb, 1959). Experiments on animals raised in a germ-free environment have suggested that the number of patches found is fixed at, or shortly after, birth, the presence of bacteria being necessary for their full development (Miyakawa, 1959). In the human being this is not the case. Peyer's patches increase in size and number throughout the second half of foetal life, and they continue to increase in size and number for at least the first 10 years after birth.

TECHNIQUES The most likely explanations for the small number of patches recorded in the textbooks are the use of degenerate material and formalin fixation.

In the present study all the material was refrigerated and obtained within a few hours of death. A separate study of refrigerated material obtained two to five days after death revealed large bile-stained and necrotic areas in the small intestines of all the cases examined. Dilute acetic acid fixation and methylene blue staining failed to demonstrate the Peyer's patches in these areas.

At the start of these investigations an attempt was made to demonstrate Peyer's patches in formalin-fixed material. Due to shrinkage of the lymphoid tissue and discoloration of the bowel wall many patches seen in the post-mortem room were no longer visible two or three days later when the formalin-fixed specimen was examined. Only large patches in the ileum could be recognized with certainty, and small patches in the duodenum and jejunum were obscured altogether. Attempts to distinguish Peyer's patches from the surrounding

tissues by differential staining techniques were unsuccessful.

The simplest way of studying Peyer's patches is to use fresh material washed in running water. If a more detailed study is required the specimen should be placed in dilute acetic acid and not in formol saline. The specimen can then be left for several weeks and the patches actually appear to improve with keeping.

SUMMARY

Thirty-eight specimens of normal small intestine from premature infants and children were examined for the presence of Peyer's patches, using acetic acid fixation and polychrome methylene blue staining.

The mean number of patches containing more than five lymphoid follicles varied from 59 before 30 weeks' gestation to 239 at puberty.

The mean number of large patches containing more than 25 follicles varied from over 40 at term to 100 or more at puberty.

Their size and number, although variable, are not fixed at birth.

They increase in size and number from early foetal life to puberty.

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