THE SEASONAL PREVALENCE OF HOFMANN'S BACILLUS[1].

By A. E. BOYCOTT, M.A., M.D.,

Fellow of Brasenose College, Oxford; Assistant Bacteriologist, Lister Institute.

(*From the Lister Institute of Preventive Medicine.*)

During the last six years (1899—1904) some fifteen thousand examinations of material from throats for the diphtheria bacillus have been made at the Lister Institute. The localities from which this material has been derived have naturally been widespread and varied; much of the work however has been done for local authorities in and near London, and the sources of origin of the major part of the material have not varied very much during the whole period under review.

Records have been kept throughout of the occurrence both of the genuine Klebs-Loeffler organism and of the pseudo-diphtheria bacillus of Hofmann. The diagnosis is based upon the microscopical appearances found in young (12—20 hours) cultures on serum made from the swabs sent to the Institute. The films are made from smears taken over the whole surface of the culture and no attempt is made to pick out individual colonies. These preparations have been made by the same laboratory attendant during the whole period dealt with here. In the ordinary routine, Loeffler's blue is alone used, though a certain number are also examined by Neisser's method. From time to time the accuracy of the diagnoses has been tested in a few instances by isolation of the organisms and investigation of the cultural and pathogenic pro-

[1] I have not attempted any survey of the literature of the subject: this has been recently reviewed in the exhaustive papers of G. S. Graham-Smith; this *Journal*, vol. III. p. 216, vol. IV. p. 258.

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TABLE I.

	A		B		C		D	
	Klebs-Loeffler per thousand of total cases examined	Percentage above (+) or below (−) mean (282)	Klebs-Loeffler per thousand of cases without Hofmann	Percentage above (+) or below (−) mean (306)	Hofmann per thousand of total cases examined	Percentage above (+) or below (−) mean (111)	Hofmann per thousand of cases without Klebs-Loeffler	Percentage above (+) or below (−) mean (142)
January	264	− 6·4	285	− 6·9	**115**	+ **3·6**	139	− 2·1
February	249	− 11·7	268	− 12·4	87	− 21·6	111	− 21·7
March	265	− 6·0	292	− 4·6	**118**	+ **6·3**	**151**	+ **6·3**
April	269	− 4·6	289	− 5·5	105	− 5·4	131	− 7·7
May	**283**	+ **0·3**	**308**	+ **0·6**	**126**	+ **13·5**	**157**	+ **10·6**
June	273	− 3·2	303	− 1·0	**128**	+ **15·3**	**164**	+ **15·5**
July	282	± 0·0	**307**	+ **0·3**	**123**	+ **10·8**	**154**	+ **8·4**
August	280	− 0·7	**311**	+ **1·6**	**144**	+ **29·7**	**181**	+ **27·5**
September	**289**	+ **2·5**	**313**	+ **2·3**	101	− 9·0	132	− 7·0
October	**321**	+ **13·8**	**345**	+ **12·7**	104	− 6·3	136	− 4·2
November	**303**	+ **7·4**	**333**	+ **8·8**	104	− 6·3	**143**	+ **0·7**
December	273	− 3·2	290	− 5·2	88	− 20·7	110	− 22·5
Average for whole period of 72 months	282		306		111		142	

The monthly percentages which are above the mean are printed in heavy type.

perties of pure cultures. Though the necessities of time and purpose have presumably led to a certain number of mistakes, the differential diagnosis between the Klebs-Loeffler and Hofmann organisms can in general be readily made by the simple method which has been used. The morphological differences are usually obvious enough, especially when taken in conjunction with the tinctorial differentiation brought out by Loeffler's alkaline methylene blue. Strictly speaking, however, the records refer to the presence of "bacilli morphologically indistinguishable from" the Klebs-Loeffler and Hofmann organisms respectively. The actual diagnoses have been made by Prof. R. T. Hewlett, Dr Sidney Rowland, Dr A. T. MacConkey, Dr A. Moore, and a few by myself, in conjunction with Dr Allan Macfadyen.

As far as possible I have eliminated from the records those cases in which swabs were taken from persons who were merely "contacts" of diphtheria infections. The remainder comprise those who were suffering either from true diphtheria or from some affection of the throat bearing a likeness to diphtheria sufficiently close to render the bacteriological examination desirable. They number in all 14937; of these

4069 or 272 per thousand showed Klebs-Loeffler alone,

1521 or 102 per thousand showed Hofmann alone,

139 or 9 per thousand showed Klebs-Loeffler and Hofmann together.

So that, in all, Klebs-Loeffler was present in 282 per thousand and Hofmann in 111 per thousand of all cases examined.

In order to investigate the question of seasonal prevalence, the proportion of examinations in which each organism was found has been calculated for each month. The details are given in the Appendix; the summarised totals are shown in Table I, and represented graphically in Fig. 1.

These show a clear difference in the seasonal variations of the frequency of positive examinations for the two organisms, *Klebs-Loeffler prevailing during September, October and November, while Hofmann is most frequent from May to August.* The curve of frequency of finding Klebs-Loeffler corresponds fairly closely with the well-known seasonal curve for the occurrence of cases of diphtheria. This points to the conclusion that the actual seasonal prevalence of Hofmann is similar to that shown in the curve of frequency of finding that bacillus in the swabs examined.

In the present series, Hofmann is much less frequently found in

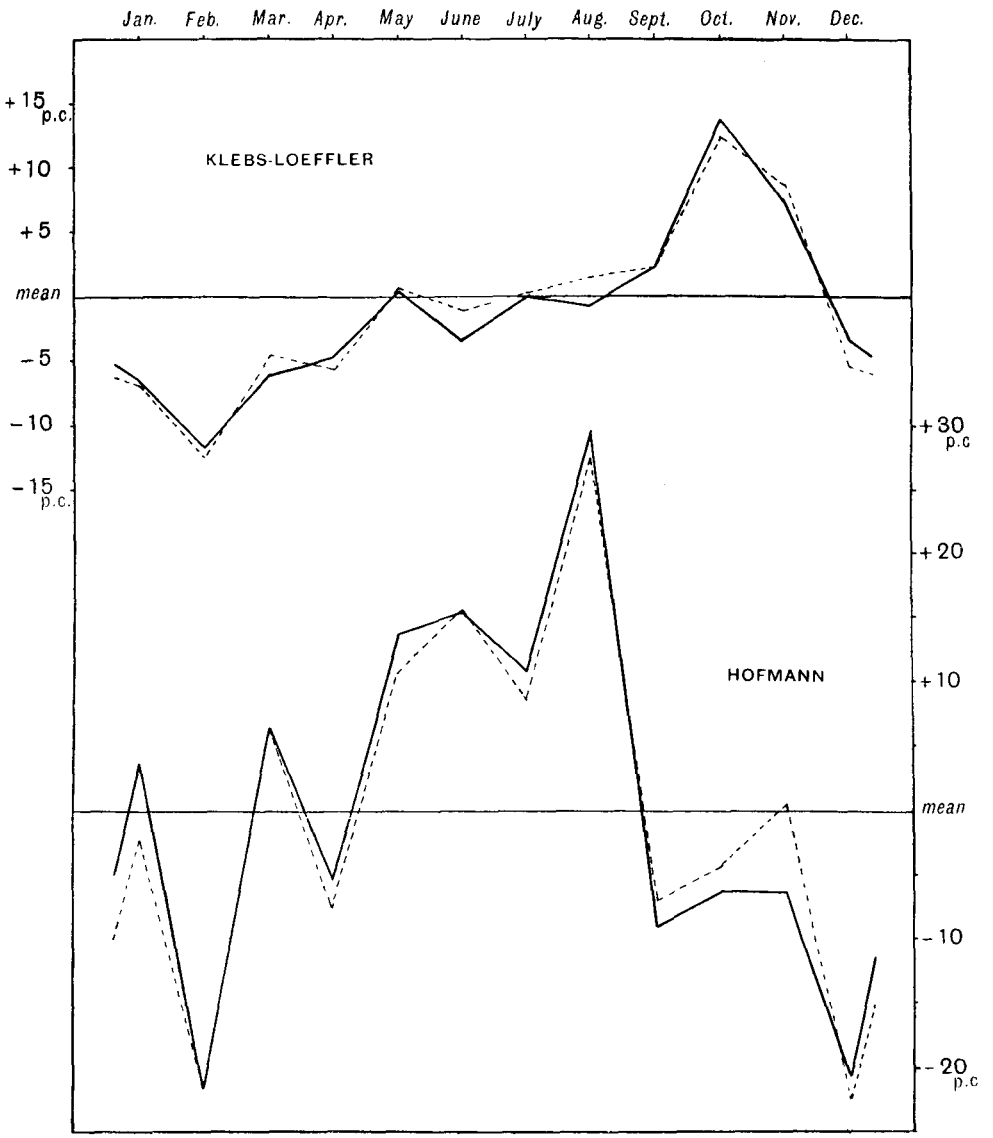

Fig. 1. The abscissae represent months; the ordinates the percentage of the mean for the whole period by which the percentage of positive examinations in each group deviates above or below the mean. The upper curves represent the proportion of Klebs-Loeffler found (1) in all cases examined (Table I, A) by the continuous line, and (2) in cases without Hofmann (Tables I, B) by the broken line.

The lower curves represent the proportion of Hofmann found (1) in all cases examined (Table I, C) by the continuous line, and (2) in cases without Klebs-Loeffler (Table I, D) by the broken line.

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cases with, than in those without Klebs-Loeffler[1]. Hence any rise in the Klebs-Loeffler curve would tend to automatically lower the Hofmann curve over the same period, if both curves are based on the percentage frequency of positive examinations in all cases examined. That this factor is immaterial in the present instance is shown by the fact that the percentage deviations of the percentages of positive results for Klebs-Loeffler in cases without Hofmann, and for Hofmann in cases without Klebs-Loeffler (Figures 1 and 2, dotted curves) correspond with those for the same organism in all cases examined.

Corresponding figures for each year are given in Table II and shown graphically in Fig. 2.

As far as the percentage of all examinations which show Klebs-Loeffler is concerned, there has been a considerable fall from 1899 (336 per thousand positive) to 1903 (180 per thousand positive) with a slight recovery in 1904. There has been no corresponding decline in the number of cases of diphtheria notified in London or in England generally during the same period. The explanation would appear to be that there has been an increasing tendency to call in the aid of bacteriology on slighter grounds, and to send swabs for examination from cases which have a more remote clinical resemblance to diphtheria.

The yearly figures for Hofmann give a curve which resembles the Klebs-Loeffler curve, though the fall has been greater throughout. If the explanation given above of the fall in the Klebs-Loeffler curve is correct, the natural conclusion to draw from the similar decline in the Hofmann curve is that Hofmann's bacillus is associated with some morbid condition of the throat which resembles, but is not identical

[1] Hofmann was found in 33 per thousand of cases with, and in 142 per thousand of cases without, Klebs-Loeffler. It is probable that these figures by no means represent, at any rate quantitatively, the real frequency of co-existence. In the first place, once Klebs-Loeffler has been found in the film, further search is not always made for Hofmann. Secondly, and perhaps most cogently, if the swab is taken accurately from a definite membrane, Klebs-Loeffler may be obtained in pure culture as being the causative organism; if Hofmann has no relation to the local disease, it would probably be absent from the acute specific local lesion. It would be interesting to know how often under these circumstances it is present in other areas of the mouth, nose and pharynx. In the third place, the possibility of the overgrowth of Hofmann by Klebs-Loeffler on a medium favourable to the latter must be considered; this does not however seem to take place in artificial mixtures grown on serum.

It may be not without significance that both organisms have been found more frequently together in monthly and yearly periods which correspond more closely with the prevalence of Hofmann than with that of Klebs-Loeffler (see Appendix, Tables G and H). The cases are however very few in number.

TABLE II.

	A		B		C		D	
	Klebs-Loeffler per thousand of total cases examined	Percentage above (+) or below (−) mean (282)	Klebs-Loeffler per thousand of cases without Hofmann	Percentage above (+) or below (−) mean (306)	Hofmann per thousand of total cases examined	Percentage above (+) or below (−) mean (111)	Hofmann per thousand of cases without Klebs-Loeffler	Percentage above (+) or below (−) mean (142)
1899	**336**	**+19·1**	**377**	**+23·2**	**163**	**+46·8**	**215**	**+51·4**
1900	**316**	**+12·1**	**353**	**+15·4**	**152**	**+36·9**	**197**	**+38·7**
1901	**324**	**+14·9**	**350**	**+14·4**	99	−10·8	139	− 9·1
1902	269	− 4·6	295	− 3·6	104	− 6·3	137	− 3·5
1903	180	−36·2	191	−37·6	67	−39·6	79	−44·4
1904	231	−18·1	242	−20·9	62	−44·1	75	−47·2
Average for whole period	282		306		111		142	

The yearly percentages which are above the mean are printed in heavy type.

with, diphtheria, and that, with a more extended use of the bacteriological test, the examples of this condition have, like those of true diphtheria, been numerically diluted by an increasing proportion of relatively normal cases. If Hofmann's bacillus were a common inhabitant of the throat, giving rise to no pathological changes, it would be natural to

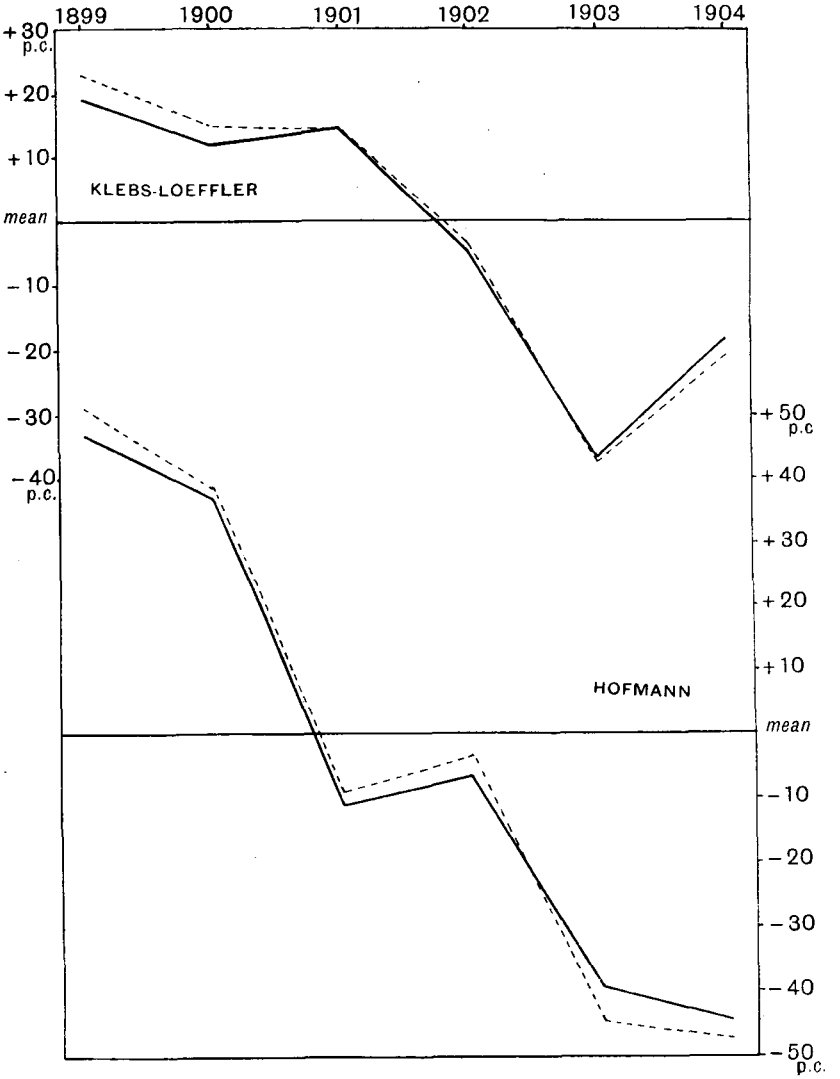

Fig. 2. The abscissae represent years. Otherwise the curves are constructed precisely as in Fig. 1, except that the vertical scale is diminished by one-half.

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suppose that the frequency of its occurrence would not materially differ from year to year, or would even have risen with the addition of a larger number of cases of mild affections. The figures may, on the other hand, merely express a general diminution in the frequency of Hofmann's bacillus, irrespective of the nature of the throats examined. The view that the similarity in the yearly curves for Hofmann and Klebs-Loeffler is to be taken as evidence of an essential and close relationship between the two organisms would correspond with an interpretation of the monthly curves as showing an aestival increase of Hofmann preparatory for, and possibly causative of, the autumnal excess of Klebs-Loeffler. Such an explanation is improbable.

APPENDIX.

TABLE A. *Total cases examined.*

Year	Jan.	Feb.	March	April	May	June	July	August	Sept.	Oct.	Nov.	Dec.	Total
1899	203	194	170	152	184	188	236	255	236	271	256	212	2557
1900	217	160	228	198	206	197	239	185	211	306	293	210	2650
1901	222	166	195	156	239	221	250	156	353	374	452	332	3116
1902	296	159	149	160	175	154	181	157	144	258	415	280	2528
1903	281	228	230	160	151	184	179	137	168	185	154	153	2210
1904	138	126	169	142	145	111	163	129	144	252	199	158	1876
Total	1357	1033	1141	968	1100	1055	1248	1019	1256	1646	1769	1345	14937

TABLE B. *Total cases in which Klebs-Loeffler was found alone.*

1899	75	61	53	42	59	51	76	65	90	76	95	63	806
1900	61	51	83	48	65	49	59	65	66	119	76	50	792
1901	69	39	49	50	62	66	73	34	125	135	165	116	983
1902	65	37	43	47	59	42	52	44	26	74	112	68	669
1903	49	30	36	46	34	38	43	36	21	21	18	22	394
1904	23	35	30	18	17	33	33	27	26	84	62	37	425
Total	342	253	294	251	296	279	336	271	354	509	528	356	4069

TABLE C. *Total cases in which Hofmann was found alone.*

1899	32	35	21	23	37	33	35	38	26	27	29	29	365
1900	46	20	38	25	27	32	26	22	25	39	47	11	358
1901	17	3	27	12	18	19	29	32	45	39	35	16	292
1902	18	12	13	11	25	19	25	20	12	27	41	30	253
1903	21	11	12	13	12	20	16	15	7	7	6	4	144
1904	5	5	16	9	5	3	7	6	3	13	19	18	109
Total	139	86	127	93	124	126	138	133	118	152	177	108	1521

TABLE D. *Total cases in which Klebs-Loeffler and Hofmann were found together.*

1899	6	0	0	4	5	3	7	4	5	9	4	6	53
1900	7	3	8	1	7	4	6	2	2	4	1	1	46
1901	2	1	0	2	2	0	1	6	1	2	0	0	17
1902	0	0	0	1	1	2	2	0	0	2	2	1	11
1903	2	0	0	0	0	0	0	1	1	0	0	0	4
1904	0	0	0	1	0	0	0	1	0	2	1	3	8
Total	17	4	8	9	15	9	16	14	9	19	8	11	139

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TABLE E. *Cases per thousand of total cases examined in which Klebs-Loeffler was found (including Klebs-Loeffler with Hofmann).*

Year	Jan.	Feb.	March	April	May	June	July	August	Sept.	Oct.	Nov.	Dec.	Total
1899	**399**	314	312	303	**348**	287	**352**	271	**402**	314	**387**	325	336
1900	313	**337**	**399**	247	**349**	269	272	**362**	**322**	**402**	263	243	316
1901	320	241	251	**333**	268	299	296	256	**347**	**366**	**365**	**349**	324
1902	219	233	**288**	**300**	**343**	**286**	**298**	**280**	180	**294**	**275**	246	269
1903	**181**	133	156	**288**	**225**	**206**	**240**	**270**	131	113	117	144	180
1904	167	**278**	177	134	117	**297**	202	217	180	**341**	**317**	**253**	231
Total	264	249	265	269	283	273	282	280	289	321	303	273	282

Percentages which are above the mean for each year are printed in heavy type.

TABLE F. *Cases per thousand of total cases examined in which Hofmann was found (including Klebs-Loeffler with Hofmann).*

1899	**187**	**180**	123	**177**	**228**	**191**	**178**	**165**	131	133	129	**165**	163
1900	**244**	144	**159**	131	**165**	**183**	134	128	128	140	**164**	57	152
1901	85	24	**138**	90	84	86	**120**	**244**	**130**	**109**	77	48	99
1902	61	75	87	75	**149**	**136**	**149**	**127**	83	**112**	104	**111**	104
1903	**82**	48	52	**81**	**79**	**109**	**89**	**116**	48	38	39	26	67
1904	36	40	**95**	**70**	34	27	43	54	21	51	**101**	**133**	62
Total	115	87	118	105	126	128	123	144	101	104	104	88	111

Percentages which are above the mean for each year are printed in heavy type.

TABLE G. *Cases per thousand of total cases examined in which Klebs-Loeffler was found with Hofmann.*

Jan.	Feb.	March	April	May	June	July	August	Sept.	Oct.	Nov.	Dec.	Total
12	4	7	9	**14**	8	**13**	**14**	7	**12**	4	8	9

1899	1900	1901	1902	1903	1904	Total
21	**17**	5	4	2	4	9

TABLE H. *Cases per thousand of cases examined with Klebs-Loeffler in which Hofmann was found.*

Jan.	Feb.	March	April	May	June	July	August	Sept.	Oct.	Nov.	Dec.	Total
47	15	26	**35**	**48**	31	**45**	**49**	25	**36**	15	30	33

1899	1900	1901	1902	1903	1904	Total
62	**55**	17	16	10	18	33

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