

phile fibrils, lysosomes, sarconemes, convoluted tubes—we prefer the last name as being least committal; they are present throughout the cytoplasm.

The nucleus shows nothing of special interest; it possesses a surface membrane and one or more nucleoli or bodies of high electron density (Figs. 4, 13). At least one large mitochondrion was found in the cystic form (Figs. 14, 15).

The cyst itself has a peculiar serrated profile and appears to be made up of the following layers (Figs. 4, 4a, 13): an outer electron-dense layer 5–10 μ m thick and an indefinite granular inner layer 200–300 μ m thick. The cyst lies in the brain tissue without provoking any reaction around it.

Discussion

Figs. 1, 2, and 3 are taken from electronmicrographs of sections of the proliferative or pseudocystic stage of *T. gondii*, and are presented here in order to effect a comparison between the two stages of the parasite. The main features are present in both forms—the conoid, paired organelles, convoluted tubes, nucleus with well-defined nucleoli, and micropyle. In the proliferated form the peripheral fibrils are less conspicuous. We have found evidence of internal budding or endodyogeny as described by Goldman *et al.* (1958) and Ludvík (1962) in this stage of the organism.

The origin of the cyst wall has been a matter of speculation for a long time. We suggest that the parasite continues to divide by internal budding, with the persistence—and enormous hypertrophy—of the pellicle of the original organism, inside which the further multiplication proceeds. The cyst wall would thus be part of the parasite itself, not derived from a host cell and therefore not “pseudocystic.” The “cogs” may be analogous to the much more developed “villi” as described by Ludvík (1960) in the cyst wall of *Sarcocystis* spp.

The presence of a micropyle in both stages of *T. gondii* is of great significance. We (Garnham *et al.*, 1961, 1962) described this structure originally in the sporozoites of malaria parasites and later in *Lankesterella*; Ludvík (1962) subsequently reported its occurrence in *Sarcocystis* and the “M-organism.” A micropyle has never been found in the flagellates, amoebae, or ciliates, and we think it may be justifiable to surmise that if a protozoon possesses such an organelle then it belongs to the Sporozoa. In view of the uncertain systematic status of *Toxoplasma*, this conclusion is of interest, because it suggests the return of *Toxoplasma* into the class where it had reposed for decades.

It was disappointing to discover no major difference between the two stages: no evidence of sexuality was found, but the life-cycle of *T. gondii* is still incompletely known, and it may yet be shown to undergo such a phase.

Summary

1. The cystic and pseudocystic (proliferative) stages of *Toxoplasma gondii* were compared under the electron microscope.

2. Both stages show the conoid, paired organelle, convoluted tubes (toxonomes), double-layered pellicle, nucleus with nucleoli, and mitochondria.

3. A single micropyle is present in both stages. Its presence suggests that *Toxoplasma* belongs after all to the class Sporozoa.

4. Peripheral fibrils are more conspicuous in the cystic stage.

5. The cyst wall is composed of a thick layer with jagged “cogs” bounded by a thin outer layer.

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CARDIAC INFARCTION AND THE GLUCOSE-TOLERANCE TEST*

BY

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The association of cardiac infarction with diabetes mellitus is well known, as is the increased insulin requirement of patients with diabetes after infarction, but the presence of latent diabetes in patients presenting with cardiac infarction is often not recognized, perhaps because it is rarely looked for.

Glycosuria during or immediately after the acute state of cardiac infarction may occur and occasionally insulin is needed for control (Cruickshank, 1931). The belief that this glycosuria is of temporary significance only was challenged by Goldberger *et al.* (1945) when they investigated 14 patients and found six with definite diabetes and four with abnormal glucose-tolerance tests. The abnormal curves sometimes took several months to develop, and most curves tended to become more diabetic as time went on, although a few returned towards normality.

In the present series the incidence of abnormal glucose-tolerance in 40 patients presenting with cardiac infarction has been investigated, together with the changes in the glucose-tolerance curves of those followed for periods of up to five years.

Method

Glucose-tolerance tests were carried out on all patients admitted under one consultant to a general hospital during one year with a diagnosis of cardiac infarction. Care was taken that these were not done, so far as could be determined, after a period of low carbohydrate intake, and it was found that the procedure did not upset ill patients. All patients were receiving the usual treatment for cardiac infarction, including anti-coagulants, and in most cases the glucose-tolerance test was carried out on the morning after admission.

The diagnosis of cardiac infarction was made on history and clinical state, E.C.G. changes, and serum glutamic oxaloacetic transaminase levels, at least two of the criteria being positive. The criteria adopted were

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very strict, and doubtful cases have been excluded. Patients with diabetes, obesity, or other known causes of an abnormal glucose-tolerance curve were excluded, as were those who did not survive two weeks. Many patients were also excluded because the diagnosis of acute cardiac infarction was not confirmed, and these were mainly suffering from ischaemic heart disease which had not produced the E.C.G. and S.G.O.T. changes characteristic of acute infarction.

A standard oral glucose-tolerance test was used, with a 50-g. dose of glucose, and venous blood-sugar levels were recorded every half-hour for two hours, while, if possible, four urine specimens were obtained at half-hourly intervals. Blood sugar levels were measured by Harding's method for "true sugar" and glucosuria was detected by the use of "clintest" tablets. Glycosuria was inconstant and unreliably related to the blood-sugar levels because of the inability of many of the patients to pass urine at the required times. Glucose-tolerance tests were repeated during convalescence and at the follow-up clinics, several patients having over four tests.

Thirteen patients who had cardiac infarctions three or more years ago, and who then had glucose-tolerance tests carried out during the acute phase, were followed up to determine what had happened to the tolerance curves: in most of these patients glucose-tolerance tests carried out during convalescence and earlier follow-up were available.

Blood cholesterol levels were also recorded in all patients.

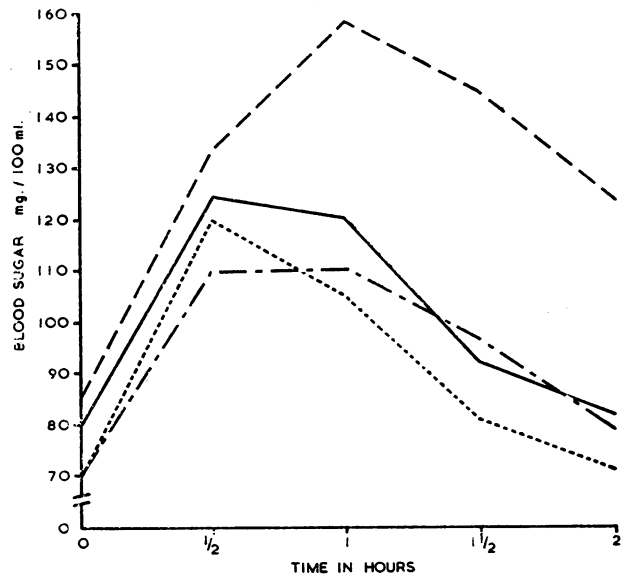
Results

Full data were available on 30 patients, and are presented in Table I. Immediately after infarction, 22 (73%) of these patients had an abnormal curve, and in 15 (50%) the curve was frankly diabetic. After six months 13 (43%) had an abnormal curve and in 3 (10%) the curve became more diabetic in seven cases, less so in 19 cases, and remained unchanged in four.

The cholesterol levels bear no relation to the glucose-tolerance curves, and range from 140 to 290 mg./100 ml., with a mean of 196 mg./100 ml. Although many patients lost weight after their infarct, they were not necessarily those whose glucose tolerance improved.

The Chart shows the mean curves of these 30 patients at different times, together with a normal curve and a composite curve from a control series of patients. The composite curves were obtained by taking the average of the readings for all relevant patients.

Controls.—Glucose-tolerance tests were carried out on 20 control patients, matched for age and sex, drawn from the same population and in the same wards: 3 (15%) had abnormal curves, but none had frankly diabetic curves. The difference between the incidence of



Mean blood-sugar curves. Acute series: ---. Six months after infarction: —. Control series: ····. Normal curve: - · - ·.

TABLE I

Case No.	Age and Sex	"Acute" G.T.T.					Follow-up G.T.T.					Type Change	Weight	Weight Change	Cholesterol (mg./100 ml.)			
		mg. "True Sugar"/100 ml.					mg. "True Sugar"/100 ml.											
1	47 M	87	128	209	168	116	D	81	93	105	93	81	N	D-N	st. lb.	-3 lb.	255	
2	52 M	87	105	139	81	87	N	70	99	70	70	58	N	N	10 9	-2 "	238	
3	59 M	105	173	168	162	142	A	58	110	64	64	58	N	A-N	10 3	-7 "	230	
4	76 F	99	110	133	200	168	D	70	128	151	116	93	A	D-A	9 11	-10 "	290	
5	63 F	70	128	174	200	128	D	93	174	157	81	58	N	D-N	11 6	-9 "	265	
6	64 F	88	127	200	170	194	D	87	145	87	64	52	N	D-N	11 12	-9 "	202	
7	54 F	75	93	87	70	52	N	70	105	70	58	58	N	Nil	9 2	-6 "	265	
8	56 M	70	128	70	75	58	N	81	151	93	93	93	A	N-A	8 13	Nil	191	
9	66 M	80	122	78	80	71	N	93	139	151	81	46	N	Nil	9 12	+5 lb.	170	
10	59 F	105	133	200	145	133	D	75	105	164	41	52	N	D-N	7 8	+4 "	205	
11	75 F	106	230	200	125	115	D	87	168	128	105	87	N	D-N	7 1	-4 "	245	
12	50 M	93	145	139	110	75	N	128	70	58	45	40	A	N-A	10 2	+2 "	244	
13	78 M	87	87	105	157	163	A	Died after three weeks										
14	81 M	99	157	200	168	145	D	81	110	99	75	87	N	D-N	9 2	-5 "	202	
15	54 M	81	139	209	215	164	D	81	133	116	116	105	A	D-A	11 1	-10 "	185	
16	58 M	96	138	203	220	190	D	70	75	93	75	58	N	D-N	12 6	-11 "	195	
17	78 M	84	158	143	122	78	N	70	122	168	116	93	A	N-A	11 0	Nil	180	
18	67 M	93	139	186	226	163	D	70	81	93	58	70	N	D-N	10 2	+5 lb.	140	
19	59 M	93	154	200	168	110	D	99	157	145	133	105	A	D-A	11 13	-2 "	190	
20	58 M	105	163	174	157	116	A	58	174	200	116	170	D	A-D	11 0	-11 "	235	
21	52 M	70	105	139	128	116	A	87	122	174	145	70	N	A-N	8 11	-2 "	210	
22	63 M	84	128	163	173	200	D	60	122	122	99	70	A	D-A	13 0	-10 "	220	
23	66 M	74	116	151	139	139	A	110	198	203	122	110	D	A-D	8 12	+12 "	220	
24	67 M	87	139	203	192	145	D	105	116	145	139	128	A	D-A	11 3	Nil	210	
25	55 M	125	192	205	110	110	D	93	151	174	139	81	N	D-N	10 0	-8 lb.	270	
26	51 M	81	122	145	133	99	A	87	116	99	41	41	N	A-N	10 12	Nil	180	
27	58 M	80	140	130	140	130	A	87	116	116	110	81	N	A-N	9 11	"	185	
28	46 M	87	151	145	87	87	N	90	130	138	118	110	A	N-A	11 3	"	200	
29	67 F	87	145	250	215	168	D	78	78	87	56	100	A	D-A	10 4	-7 lb.	195	
30	40 F	76	58	52	64	52	N	70	75	120	80	64	N	Nil	10 6	Nil	200	
31	57 M	35	151	158	116	100	A	90	209	133	139	130	D	A-D	10 0	-5 lb.	190	
Composite		87	134	159	147	124		83	126	121	93	82						

N=Normal. A=Abnormal. D=Diabetic. * Glucose-tolerance test. Values in mg. of "true sugar" per 100 ml. † Cholesterol in mg./100 ml.

abnormal curves in the control series and the infarct series after six months is 28%, while a difference of up to 24% would be expected by chance (5% significance level).

Follow-up Series.—The results on the 13 patients followed up for at least three years are shown in Table II. Eight (62%) of these patients had abnormal curves in the acute phase, of which four (30%) were diabetic. By the time of the follow up four (30%) patients had abnormal curves, two (15%) having developed clinical diabetes.

of which the best-known are emotion (Barach, 1950), trauma, especially fractures, and infection.

It is very rare for insulin to be needed to control the abnormal glucose metabolism, and, as Raab and Rabinowitz point out, insulin can be extremely dangerous if given to a patient with ischaemic heart disease, especially if he has just had a cardiac infarction. Insulin may cause hypoglycaemia, leading to severe angina or further infarction, and may also lead to arrhythmias, possibly by its effect on cardiac potassium levels.

TABLE II

No.	Age	Sex	Acute G.T.T.					Type	Chol.	Follow-up G.T.T.					Type	Chol.	Years	Change in Wt.	
28	46	M	87	151	145	87	87	N	200	93	151	209	151	116	D	200	3	6	Nil
29	67	F	87	145	250	215	168	D	195	90	110	153	130	110	A	243	3	0	-7 lb.
30	40	F	76	58	52	64	52	N	200	64	70	96	70	60	N	185	3	8	Nil
31	57	M	35	151	158	116	100	A	190	120	240	190	158	130	D	190	3	6	-5 lb.
32	66	M	91	126	161	200	184	D	174	70	105	116	93	70	N	295	3	0	-5 "
33	49	M	64	105	128	116	100	A	—	80	105	163	128	80	N	187	3	8	+14 "
34	68	M	70	81	93	93	105	A	—	93	145	116	87	64	N	195	3	0	+2 "
35	50	F	116	232	180	151	159	D	157	80	81	128	116	81	N	165	4	10	+7 "
36	66	M	87	105	128	105	86	N	—	93	105	128	145	140	A	290	3	2	Nil
37	60	F	87	139	139	128	139	A	185	81	116	105	81	70	N	230	5	0	-12 lb.
38	57	M	104	151	168	203	139	D	188	75	145	99	64	75	N	200	3	6	Nil
39	47	M	87	157	122	87	46	N	156	99	157	105	70	60	N	250	3	5	Nil
40	53	M	70	174	139	99	70	N	—	70	105	99	52	58	N	250	3	6	+3 lb.

Discussion

W. Oakley's (1959, personal communication) view is that a normal glucose-tolerance curve has a fasting level of not over 110 mg./100 ml., a peak of not over 180 mg./100 ml., and must return to the fasting level at two hours; abnormal curves may be of three types, with a high fasting level, delayed return, or a high peak, and on further investigation some of these patients are found to have no diabetic tendency.

In this study a curve is classified as normal if (1) the fasting level is not higher than 110 mg./100 ml., (2) the peak level is not higher than 180 mg./100 ml., (3) the two-hour level is not higher than the fasting level, and (4) there is no glycosuria. A curve is classified as diabetic if (1) the peak is over 220 mg./100 ml., (2) the fasting level is over 120 mg./100 ml. with a peak of 200 mg./100 ml., or (3) the peak is 200 mg./100 ml. with a delayed return to the fasting level. Curves falling between the criteria for "normal" and those for "diabetic" are classified as abnormal.

Cause of Abnormal Curves.—There are six main theories regarding the cause of the abnormal curves. (1) Increased adrenal cortical steroid production as a response to stress. This theory does not explain those cases in which the curve does not rapidly return to normal. (2) A circulatory disturbance in the brain with functional changes in the hypothalamic region (Raab and Rabinowitz, 1936). This explains only short-term abnormalities. (3) Increased adrenaline release causing excess glycogenolysis. This theory also fails to explain the persistence of the abnormality. (4) Low-carbohydrate diet before the test may cause altered carbohydrate tolerance. This may be the cause of some of the curves found in the acute phase, although efforts were made to avoid this error; it does not explain persisting abnormalities. (5) Changes in the liver following shock upset carbohydrate metabolism (Ellenberg *et al.*, 1952). This will explain only the early abnormalities. (6) The infarct precipitates latent diabetes. This is the most satisfactory explanation, as it accounts for both the early and the late abnormalities. Many authors have described other precipitating factors,

Summary and Conclusions

Glucose-tolerance tests have been carried out immediately after cardiac infarction in 40 patients; follow-up tests have been carried out on 30 patients after six months and on 13 patients after periods of up to five years.

Immediately after cardiac infarction, 22 (73%) of the 30 patients had abnormal glucose-tolerance curves; after six months 13 (43%) had abnormal curves.

At least three years after a cardiac infarct 4 (27%) out of 15 patients had abnormal curves, of whom 2 (13%) had developed clinical diabetes.

The development of abnormal curves was not related to the level of blood cholesterol, nor to weight changes.

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"Children admitted to hospital for the special medical treatment which cannot be provided at home are visited regularly by health visitors, who consult with the hospital medical staff and ward sisters, about the after-care of the child when due to be discharged. As a result of this interchange of information concerning the home and social conditions of these children, some cases are able to be discharged home earlier to the care of their mother. The health visitor then acts under the direction of the family doctor. Where further skilled nursing attention is required, the health visitor explains to the mother how to obtain this through the District Nursing Service. Excellent co-operation exists between the family doctor and the health visitor and, where conditions are suitable, sick children are nursed at home, again using the District Nurses where necessary. Domestic help is also available where required." (*Annual Report of Medical Officer of Health, County Borough of Swansea.*)