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OBSERVATIONS ON THE INFLUENCE OF  
NUCLEIC ACID UPON LEUCOCYTOSIS.

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Being a Thesis for the Degree of M.D.

by

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Before certain operations and especially in those in which the peritoneal cavity is opened, some surgeons have advocated the administration of chemical substances to the patient whereby a leucocytosis or hyperleucocytosis may be provoked in order to act as a prophylaxis against any subsequent sepsis, and also to aid the patient to combat against which should such arise. Amongst such chemical substances employed may be mentioned Nucleic Acid.

It came within my experience to employ Nucleic Acid for such conditions; and results which I obtained from its use prompted me later to make investigations on its influence upon leucocytosis. Accordingly at a later date I undertook experiments upon 36 cases; and the results and conclusions at which I arrived will be given in the following sheets.

Methods employed:

The methods which I employed were as follows:-

- I. The cases for investigation were divided up into 3 groups or series. Series A. B. C.
- II. In series A. 12 patients were each injected hypodermically with 60 minims of a 5% solution of Nucleic Acid from yeast prepared by Parke, Davis & Co. A Leucocyte count was obtained prior to the hypodermic injection, and/

and also, 12 hours after injection.

The Differential Counts were also obtained on both occasions.

III. In Series B. 12 patients were each injected as in Series A, with 60 minims of a 5% solution Nucleic Acid (as above). Leucocyte and Differential Counts were taken prior to injection, and at intervals of 2, 4, 6, and 12 hours after injection.

IV. In Series C. 12 patients were each injected as in Series A. and B. with 20 minims of a 5% solution Nucleic Acid (as above). Leucocyte Counts were taken prior to injection, and at intervals of 2, 4, and 12 hours after injection. Differential Counts were obtained before injection, and 2, and 12 hours after injection.

V. The period of experiment lasted generally between 10 P.M. and 10 A.M. Commencing at 10 P.M. no acute symptoms were present before experiment in any case.

VI. Patients for investigation were given a light/

light supper of bread and Butter and milk at 8 P.M. Breakfast was given at 8 A.M. and consisted of porridge or an egg, and a cup of weak tea and bread and butter. At 5 A.M. however each patient partook of a cup of milk and a slice of bread and butter.

### Technique.

Strict antiseptic precautions were observed, both in regard to the instruments employed, and the site for injection selected. Injection was made in every case at the shoulder above the Deltoid muscle.

I propose now, to give in order, the results obtained from Leucocyte and Differential Counts of the three Series:- A. B. C. respectively. An epitome of the history of each case in the three series would be both welcome and instructive.

### SERIES A.

Case I.    Male aet 52.    Commercial Traveller.

Gastric and Pyloric Carcinoma.    First complained of pain in stomach and diarrhoea after an indiscreet diet. Vomited six weeks before he was admitted to hospital. Clear fluid vomited. No Haematemesis nor Melaena. Had been troubled previously with "Neurasthenic Headaches due to business worries." Otherwise previous health was good; /

good; as also were his family history and social condition and habits. Although he had lost 20 lbs. weight in 3 months he did not appear emaciated to any degree. Gastro-Pylorotomy performed. Glands in Omentum found enlarged. No Hepatic invasion detected. Convalesced satisfactorily.

Leucocytes before Nucleic Acid 7900.

Leucocytes after Nucleic Acid 22,600.

Differential Count in percentage.

	<u>Before</u>	<u>After</u>
Polymorphs	61.5%	62.7%
Lymphocytes	33.5%	28.5%
Large Mononuclears	2.4%	5.5%
Eosinophiles	.8%	-
Basophiles	-	-
Transition Polymorphs	1.8%	3.3%

Case II. Male aet 35. Joiner.

Tuberculous Strictures (10) of Small Intestine:

History of pain in stomach, and vomiting  $1\frac{1}{2}$  hours after food. Duration 22 months. Constipation 10 months. Progressive loss of weight. Treated with medicines and by Gastric lavage with very slight benefit. Laparotomy later. Anterior Gastro-Enterostomy/

Enterostomy. No improvement while at a Convalescent Home. His medical attendant wrote later. "He rapidly emaciated with a high temperature. Haematemesis occurred the day before death and he soon sank." No Pulmonary complication was present while he was in hospital. If so, it was not detectable.

Leucocytes before Nucleic Acid 7900.

Leucocytes after Nucleic Acid 12,700.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs.	61.0%	66.6%
Lymphocytes	29.5%	21.3%
Large Mononuclears	3.2%	6.0%
Eosinophiles	1.8%	1.1%
Basophiles	-	-
Transition Polymorphs	4.5%	5.0%

Case III. Male aet 48. Stone Cutter.

Carcinoma Sigmoid, adherent to Bladder.

Complained of constipation and **gripping** pains in abdomen of 8 weeks duration. Pains eased on passage of Flatus. Melaena. No vomiting. Urine contained blood at times. Lost 5 lbs. weight within a week.  
Double/

Double Enterectomy and Colostomy done. Died suddenly 2 days after operation. Post-mortem revealed Colloid Cancer. No Peritonitis present.

Leucocytosis before Nucleic Acid 11800.

Leucocytosis after Nucleic Acid 11600.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	63.6%	61.8%
Lymphocytes	27.3%	16.5%
Large Mononuclears	6.6%	18.7%
Eosinophiles	-	1.0%
Basophiles	-	-
Transition Polymorphs	2.5%	2.0%

Case IV.      Male aet 46.      Painter.

Recommended as a case of Gastric Carcinoma. Laparotomy performed but nothing of such nature found. Pneumonia occurred after operation and death took place on 5th day. Post-mortem revealed great anaemia and pallor of viscera and iron pigment was present in the Liver and Spleen,- suggesting Pernicious Anaemia; though examination of blood previously before death did not suggest such.

Leucocytes before Nucleic Acid 4600

Leucocytes after Nucleic Acid 5100

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	75.1%	80.9%
Lymphocytes	12.5%	14.5%
Large Mononuclears	8.8%	3.2%
Eosinophiles	.8%	.5%
Basophiles	-	-
Transition Polymorphs	2.8%	.9%

Case V. Female aet 20. Domestic Servant.

Relapsing Appendicitis. Appendectomy.

Previous health and habits good. Cured.

Leucocytes before Nucleic Acid. 9800.

Leucocytes after Nucleic Acid 22.600.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	50.3%	75.3%
Lymphocytes	40.7%	14.9%
Large Mononuclears	6.6%	4.9%
Eosinophiles	.5%	-
Basophiles	-	-
Transition Polymorphs	1.9%	4.9%

Case VI. Female aet 56. Housewife.

History of Dyspepsia and general weakness.

Vomiting/

Vomiting and Constipation of 12 months duration. Lost 70 lbs. weight in six months previous to admission to hospital. Free Hydrochloric Acid in Test Meal. Laparotomy performed. Nothing abnormal found.

Leucocytosis before Nucleic Acid 4300

Leucocytosis after Nucleic Acid 19500

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	52.4%	80.9%
Lymphocytes	36.3%	12.7%
Large Mononuclears	6.0%	2.7%
Eosinophiles	3.3%	-
Basophiles	-	-
Transition Polymorphs	2.0%	3.7%

Case VII. Male aet 23. Bank Clerk.

Tubercle of Small Intestine, Coecum, Appendix.

Had two attacks of what was supposed to be Appendicitis. Operation in a quiescent period showed the condition above named. Enterectomy performed. Glands in mesentery tuberculous. Convalescence satisfactory. Gained in weight.

Leucocytosis before Nucleic Acid 11800

Leucocytosis after Nucleic Acid 9300

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	51.9%	73.6%
Lymphocytes	33.1%	17.5%
Large Mononuclears	8.9%	7.9%
Eosinophiles	2.2%	=
Basophiles	-	.1%
Transition Polymorphs	3.9%	.9%

Case VIII. Male aet 36. Clerk.Chronic Gastric Ulcer and Pyloric Stenosis.

Complained of severe pain in stomach for 7 weeks. Similar attacks 10 years previously when there was haematemesis. No tenderness on pressure. Stomach extended to  $1\frac{1}{2}$  inches below level of Umbilicus. Free Hydrochloric Acid present in Test Meal. Gastro-Enterostomy. Cicatricial contraction on upper surface of Pylorus. Non malignant enlarged omental glands.

Leucocytosis before Nucleic Acid 10,000.

Leucocytosis after Nucleic Acid 19,400.

Differential Count:/

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	54.6%	80.8%
Lymphocytes	36.6%	14.5%
Large Mononuclears	7.6%	2.3%
Eosinophiles	.5%	.4%
Basophiles	-	.4%
Transition Polymorphs	.7%	1.6%

Case IX. Female aet 61. Farm Servant.

Colloid Cancer of the Peritoneum.

Gradual enlargement of the Abdomen had been perceived for  $2\frac{3}{4}$  years. There was no pain. Had dragging pains later in the back and at intervals. Did not lose weight. 1 child died of Phthisis.

Leucocytosis before Nucleic Acid 4700.

Leucocytosis after Nucleic Acid 9100.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	64.0%	84.5%
Lymphocytes	20.0%	9.0%
Large Mononuclears	6.4%	2.4%
Eosinophiles	6.1%	.8%
Basophiles	.8%	-
Transition Polymorphs	2.7%	3.3%

Case X.      Male aet 24.      Groom.

Recurrent Appendicitis. 3 Attacks. Cured.

Family History, previous health, social condition and habits satisfactory.

Leucocytosis before Nucleic Acid 9400.

Leucocytosis after Nucleic Acid 18600.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	51.4%	84.1%
Lymphocytes	39.6%	9.3%
Large Mononuclears	3.6%	2.8%
Eosinophiles	1.9%	.7%
Basophiles	.6%	-
Transition Polymorphs	2.9%	3.1%

Case XI.      Male aet 16.      Joiner.

Recurrent Appendicitis. 3 attacks. Cured.

Pleurisy and Pneumonia when aet 12. Family History and social habits satisfactory.

Leucocytosis before Nucleic Acid 6300.

Leucocytosis after Nucleic Acid 17600.

Differential Count: /

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	47.6%	73.4%
Lymphocytes	47.9%	19.1%
Large Mononuclears	1.5%	4.7%
Eosinophiles	1.5%	1.6%
Basophiles	-	-
Transition Polymorphs	1.5%	1.2%

Case XII. Female aet 54. Housewife.

Carcinoma Ascending Colon: Enterectomy.

History of Chronic Constipation for 2 years, later becoming acute. Showed little emaciation and looked healthy.

Leucocytosis before Nucleic Acid. 8000

Leucocytosis after Nucleic Acid 18700.

Differential Count:

	<u>Before</u>	<u>After</u>
Polymorphs	72.2%	76.0%
Lymphocytes	15.6%	18.6%
Large Mononuclears	7.5%	3.7%
Eosinophiles	1.3%	.5%
Basophiles	-	-
Transition Polymorphs	3.4%	1.2%

SERIES B.

Case I. Male aet 19. Fisherman.

Tuberculous disease of Knee Joint. Excision.

Troubled with knee for 4 years. Previously had always enjoyed good health. No tuberculous disease elsewhere in body. Strong and muscular. Strong Tuberculous diathesis in relatives.

Leucocytosis	Before	2.	4.	6.	12 hours after.
	7600	8200	12260	14600	14600

Differential Count:

Hours after

	Before	2.	4.	6.	12.
Polymorphs	46.5%	51.6%	64.6%	67.1%	65.7%
Lymphocytes	39.8%	33.3%	31.5%	24.2%	26.5%
Large Mononuclears	6.3%	6.0%	.3%	4.4%	3.9%
Eosinophiles	4.6%	4.3%	1.2%	2.2%	2.3%
Basophiles	.9%	.5%	-	.6%	.3%
Transition Polymorphs.	1.9%	4.3%	2.4%	1.5%	1.3%

Case II. Male aet 19. Cable Car Workshop.

Sustained accident whereby foot was crushed.

History of glands in neck being removed in childhood; and an abscess in axilla being opened. Family history satisfactory.

Leucocytosis/

Leucocytosis	Before	2	4	6	12 hours
	10900	7300	12200	12000	18500

Differential Count:

hours after

	Before	2	4	6	12 hours
Polymorphs	59.2%	58.6%	65.5%	73.0%	74.3%
Lymphocytes	32.2%	32.8%	26.2%	18.2%	15.8%
Large Mono-nuclears	4.9%	3.5%	4.2%	5.6%	7.9%
Eosinophiles	1.2%	2.2%	1.6%	.7%	.8%
Basophiles	-	.7%	-	.6%	-
Transition Polymorphs	1.9%	2.2%	2.5%	1.9%	1.2%

Case III. Male aet 43. Butcher.Comminuted Pott's Fracture. Had Acute Bright's

Disease 4 years previously due to drink and exposure.

Influenza some years previous to Bright's. Family history satisfactory.

Leucocytosis	Before	2	4	6	12 hours.
	12500	13100	3900	12100	13400

Differential Count: /

Differential Count:

	Before	hours after			
		2	4	6	12 hours
Polymorphs	67.6%	76.3%	75.5%	81.6%	84.4%
Lymphocytes	23.7%	16.1%	14.7%	11.4%	9.9%
Large Mono-nuclears	5.0%	4.3%	6.7%	4.3%	3.4%
Eosinophiles	2.0%	1.2%	1.9%	.8%	.5%
Basophiles	-	.6%	-	-	-
Transition Polymorphs	1.7%	1.5%	1.2%	1.3%	1.8%

Case IV. Male aet 18. Apprenticed Workman.Tuberculous Disease. Ankle. Amputation.

Disease commenced about 2 years previously. Had measles and scarlet fever in childhood. Mother and one brother (aet 21) died of Phthisis.

Leucocytosis	Before	2	4	6	12
	6300	8800	11200	11000	155000

Differential Count:

	Before	hours after			
		2	4	6	12
Polymorphs	40.3%	49.0%	28.4%	73.3%	66.9%
Lymphocytes	50.4%	46.9%	66.1%	18.3%	29.7%
Large Mono-nuclears	5.9%	1.3%	3.4%	3.5%	1.3%
Eosinophiles	1.2%	.2%	.5%	-	-
Basophiles	.7%	-	-	-	-
Transition Polymorphs	1.5%	1.6%	1.6%	2.5%	2.1%

Case V. Female aet 35. Housework.Varicose Veins present for 24 years.

Getting worse. Measles and fever in childhood, otherwise healthy. Non Tuberculous. Father died (aet 28) Phthisis. Mother died Pneumonia. Patient has good habits and healthy surroundings.

Leucocytosis	Before	2	4	6	12
	7300	6400	8000	7100	7600

Differential Count:

hours after

	Before	2	4	6	12
Polymorphs	58.3%	57.2%	51.2%	56.9%	61.3%
Lymphocytes	37.2%	35.4%	45.5%	39.5%	35.9%
Large Mono-nuclears	.9%	1.2%	.9%	.5%	.2%
Eosinophiles	2.2%	3.1%	1.2%	1.2%	.9%
Basophiles	-	.6%	-	-	.2%
Transition Polymorphs	1.2%	2.5%	1.2%	1.9%	1.5%

Case VI. Female aet 28. Housewife.Tuberculous Strictures (10) Small Intestine.

For three years used to suffer from Flatulence and pain. Mass palpable towards right of Umbilicus. Lateral Anastomosis performed. Developed a Thrombosis of Left Internal Saphenous vein after operation. Improved. No Tuberculous disease in family. Recovered.

Leucocytosis/

Leucocytosis	Before	2	4	6	12
	4600	6200	4600	6400	5700
<u>Differential Count:</u>		Hours after			
	Before	2	4	6	12
Polymorphs	50.6%	57.4%	52.6%	45.7%	62.2%
Lymphocytes	40.3%	36.6%	41.0%	44.6%	30.3%
Large Mono-nuclears	4.0%	1.9%	5.9%	4.0%	3.0%
Eosinophile	.8%	-	-	1.7%	2.3%
Basophiles	-	-	-	-	-
Transition Polymorphs	4.3%	4.1%	1.4%	4.0%	.2%

Case VII. Male aet 40. Crofter.

Chronic Periostitis Tibia of 30 years duration.

Good family history. Takes alcohol in moderation.

Open air life. Bone trephined. Cured.

Leucocytosis	Before	2	4	6	12
	26200	15400	11100	12400	15800
<u>Differential Count:</u>		Hours after			
	Before	2	4	6	12
Polymorphs	66.0%	72.2%	54.6%	75.0%	78.2%
Lymphocytes	26.4%	22.9%	35.0%	19.0%	16.4%
Large Mono-nuclears	2.6%	1.8%	3.0%	1.7%	1.9%
Eosinophiles	1.4%	.2%	4.0%	.8%	.9%
Basophiles	-	.2%	-	-	.9%
Transition Polymorphs	3.6%	2.7%	3.4%	3.5%	1.7%

Case VIII. Male aet 28. Railway Platelayer.Tuberculosis of Prostate, Bladder Epididymis.

Frequency of Micturition for 6 months. No haematuria nor pain at first. 12 months previously had accident to Perineum when jumping a fence - subsequent haematuria for three days. Influenza when aet 20. No Tuberculous history in family given. Urine showed Albumin and "swarmed with Tubercle Bacilli." Later developed Miliary Tuberculosis of the Lungs and uraemia and died.

Leucocytosis.	Before	2	4	6	12
	9600	12800	11400	17000	21000

Differential Count:

	Before	hours after			
		2	4	6	12
Polymorphs	76.3%	74.7%	81.9%	84.3%	81.3%
Lymphocytes	15.3%	19.0%	13.1%	7.8%	10.0%
Large Mono-nuclears	3.5%	4.0%	3.2%	4.5%	4.3%
Eosinophiles	.5%	-	-	-	-
Basophiles	-	-	-	-	-
Transition Polymorphs	4.4%	2.3%	1.8%	3.4%	4.4%

Case IX. Male aet 36. Cooper.

Chronic Gastric Ulcer and Haematemesis of three years duration. No Melaena. Adhesions found between Liver and Stomach. Small Calcareous plate on Anterior/

Anterior surface of stomach. Posterior Gastro-Enterostomy. Cured. Good family history.

Leucocytosis	Before	2	4	6	12
	13400	11800	11000	12800	4100

Differential Count:

	Before	Hours after			
		2	4	6	12
Polymorphs	29.8%	17.9%	33.0%	54.2%	67.8%
Lymphocytes	64.9%	76.4%	62.0%	30.4%	25.1%
Large Mono-nuclear	2.5%	5.7%	-	4.2%	2.5%
Eosinophiles	.9%	-	3.0%	1.8%	-
Basophiles	-	-	.9%	-	-
Transition Polymorphs	1.9%	-	2.0%	8.5%	4.6%

Case 10. Male aet 56. Iron Moulder.

Proctitis. Chronic nature and of 9 years duration Melaena for same period. Good family history. Habits satisfactory. Cured.

Leucocytosis	Before	2	4	6	12
	10200	5400	5500	6100	22800

Differential Count:/

## Differential Count:

hours after

	Before	2	4	6	12
Polymorphs	49.2%	56.4%	35.6%	73.6%	85.0%
Lymphocytes	50.7%	39.5%	57.5%	25.0%	14.0%
Large Mono-nuclears	-	4.5%	4.1%	.6%	-
Eosinophiles	-	-	-	-	-
Basophiles	-	-	-	-	-
Transition Polymorphs	.1%	.6%	2.6%	.6%	1.0%

## Case XI. Female aet 44. Seamstress.

Chronic Gastric Catarrh and weakness of 15 years duration. Also a fibroid uterus which was not removed on account of general weak condition.

Infantile Paralysis aet 16 months. Gastric derangement improved under dietary and medicinal treatment. Gained  $4\frac{1}{4}$  lbs. weight in 26 days.

Leucocytosis	Before	2	4	6	12
	7900	9200	10800	27500	28200.

## Differential Count:

hours after

	Before	2	4	6	12
Polymorphs	63.0%	44.0%	61.4%	70.3%	79.6%
Lymphocytes	32.4%	18.4%	46.1%	34.8%	25.8%
Large Mono-nuclears	2.5%	9.0%	2.0%	3.2%	1.2%
Eosinophiles	-	-	.8%	-	-
Basophiles	-	-	-	-	-
Transition Polymorphs.	2.1%	.9%	1.0%	.7%	.8%

Case XII. Male aet 50. Engineer.Epithelioma of Tongue and Soft Palate.

Commenced as a small blister 5 weeks previously ,  
ulcer formed later. Half of tongue and adjacent  
soft palate affected. Secondary enlarged Cervical  
Glands. "Ague" when aet 15. Heavy smoker. Moderate  
in alcohol. Family history satisfactory. Relieved.

Leucocytosis	Before	2	4	6	12
	14200	14000	16700	15700	14800
<u>Differential Count:</u>		Hours after			
	Before	2	4	6	12
Polymorphs	71.7%	69.8%	64.5%	61.4%	65.5%
Lymphocytes	23.1%	22.2%	26.7%	32.3%	27.7%
Large Mono-nuclears	2.5%	4.4%	7.0%	3.8%	3.6%
Eosinophiles	.3%	1.4%	.6%	-	.6%
Basophiles	-	-	-	-	-
Transition Polymorphs	2.2%	2.2%	1.2%	2.5%	2.6%

SERIES C.Case I. Male aet 52. Fireman.

Gastric Carcinoma, involving Lesser Curvature  
and Anterior Surface of Stomach. Glands also  
involved. No free Hydrochloric Acid in Stomach.

Mother/

Mother died aet 58 insane. One brother died aet 34, Malaria. Operation relieved patient. Haematuria developed later.

Leucocytosis.	Before	2	4	12
	5300	5800	8300	10200
<u>Differential Count:</u>		Hours After		
	Before	2	12	
Polymorphs	63.6%	69.4%	77.6%	
Lymphocytes	31.6%	12.3%	14.8%	
Large Mononuclears	2.3%	10.4%	3.8%	
Eosinophiles	.5%	1.5%	1.6%	
Basophiles	-	1.2%	1.0%	
Transition Polymorphs.	2.0%	5.2%	1.2%	

Case II. Male aet 54. Carrier.

Malignant disease of Oesophagus. Oesophageal obstruction of 5 months duration. Enlarged glands below left clavicle. Lost 3 lbs. weight in 14 days. Gastrostomy gave relief.

Leucocytosis.	Before	2	4	12
	13600	18200	22600	24200
<u>Differential Count:/</u>				

Differential Count.

	Before	Hours after	
		2	12
Polymorphs	77.5%	75.5%	81.4%
Lymphocytes	14.7%	20.1%	10.7%
Large Mononuclears	4.8%	-	5.2%
Eosinophiles	.8%	-	.5%
Basophiles	-	-	-
Transition Polymorphs.	2.2%	4.4%	2.2%

Case III. Male aet 48. Scavenger.

Tuberculous Teno-Synovitis and Ankle. Foot amputated. Tuberculous Synovial sheath excised 6 months previously. Family history satisfactory.

Leucocytosis.	Before	2	4	12
	6800	6400	8800	12000

Differential Count:

	Before	Hours after	
		2	12
Polymorphs	30.7%	58.6%	65.4%
Lymphocytes	54.8%	20.4%	23.7%
Large Mononuclears	10.2%	12.5%	7.5%
Eosinophiles	1.3%	1.7%	-
Basophiles	-	-	-
Transition Polymorphs.	3.0%	6.8%	3.4%

Case IV. Male aet 64. Labourer.

Painful/

Painful Stump due to Neuromata accident to hand necessitated amputation. Had always been healthy. No disease in Family History.

Leucocytosis	Before	2	4	12
	14400	9100	11800	29900

Differential Count:

Hours after

	Before	2	12
Polymorphs	44.7%	41.6%	77.7%
Lymphocytes	44.7%	40.6%	14.5%
Large Mononuclears	7.0%	12.6%	2.2%
Eosinophiles	1.2%	2.9%	.4%
Basophiles	.5%	-	.3%
Transition Polymorphs.	1.9%	2.9%	4.9%

Case V. Male aet 24. Steel worker.

Pain and stiffness of Right Hip Joint of 12 months duration. No abnormality nor disease present when exploratory incision was made.

Leucocytosis	Before	2	4	12
	11600	8400	5100	12400

Differential Count/

Differential Count:

	Before	Hours after	
		2	12
Polymorphs	55.0%	59.2%	84.7%
Lymphocytes	28.8%	36.1%	6.6%
Large Mononuclears	6.3%	2.6%	4.4%
Eosinophiles	3.9%	.9%	1.2%
Basophiles	.6%	-	-
Transition Polymorphs.	5.4%	1.2%	3.1%

Case VI. Male aet 30. Gymnast.

Pain and weakness in back of 2 months duration.

Strained back at Gymnastics. Typhoid 12 years previously. Exaggerated Knee Jerks and Ankle Clonus suggested condition being Pott's disease of the Spine. Ordered rest in bed and counter irritation along the spine. Improved.

Leucocytosis	Before	2	4	12
	9100	11400	11900	18400

Differential Count:

	Before	Hours after	
		2	12
Polymorphs	41.9%	46.7%	83.9%
Lymphocytes	41.9%	39.4%	6.8%
Large Mononuclears	8.0%	6.9%	4.7%
Eosinophiles	4.5%	3.9%	.6%
Basophiles	.5%	-	-
Transition Polymorphs.	3.2%	3.1%	4.0%

Case VII. Male aet 55. Miner.

Epithelioma of Cheek and Upper Jaw. Operated on two occasions due to recurrence. Glands in neck also involved. Had been a heavy smoker and moderate drinker. One sister died Intestinal obstruction. Patient relieved after second operation.

Leucocytosis	Before	2	4	12
	6100	7600	6100	13600

Differential Count:

	Before	Hours after	
		2	12
Polymorphs	56.9%	60.2%	74.0%
Lymphocytes	39.7%	24.0%	18.9%
Large Mononuclears	1.1%	8.0%	4.8%
Eosinophiles	-	3.6%	.6%
Basophiles	-	-	-
Transition Polymorphs	2.3%	4.2%	1.7%

Case VIII. Male aet 24. Labourer.

Tuberculous Cervical Glands on both sides of neck. Recurrence necessitated two operations. Tuberculous Family History. Father died aet 48 Typhoid. Patient convalesced well. Relieved.

Leucocytosis	Before	2	4	12
	9300	12600	16200	38200

Differential Count: /

Differential Count:	Hours after		
	Before	2	12
Polymorphs	60.4%	71.3%	76.8%
Lymphocytes	30.5%	19.3%	16.0%
Large Mononuclears	4.9%	6.4%	3.5%
Eosinophiles	.6%	.9%	-
Basophiles	-	-	-
Transition Polymorphs.	3.6%	2.1%	3.7%

Case IX.      Male aet 54.      Fisherman.

Complained of Chronic Cystitis but nothing abnormal in urine to corroborate diagnosis.

Complained also of pain in stomach and side (left) and constipation. Prostatectomy 2 years previous to admission. Treated as Gastric Neurosis. Relieved.

Leucocytosis.	Before	2	4	12
	6400	6000	8000	10200

Differential Count:	Hours after		
	Before	2	12
Polymorphs	31.2%	39.8%	61.9%
Lymphocytes	62.4%	46.0%	32.1%
Large Mononuclears	5.3%	11.1%	3.7%
Eosinophiles	1.1%	1.6%	1.1%
Basophiles	-	.7%	-
Transition Polymorphs.	-	.8%	1.2%

Case X./

Case X. Female aet 49. Housewife.

Anal Fissure 2 years duration. Satisfactory  
Family History etc. Cured.

Leucocytosis	Before	2	4	12
	11500	9800	9600	16600

Differential Count:

	Before	Hours after	
		2	12
Polymorphs	51.6%	63.9%	76.3%
Lymphocytes	41.0%	29.4%	16.6%
Large Mononuclears	3.0%	2.8%	2.7%
Eosinophiles	3.0%	2.1%	1.5%
Basophiles	-	-	.5%
Transition Polymorphs	1.4%	1.8%	2.4%

Case XI.. Male aet 19. Miner.

Supposed Vesical Calculus. History of having passed a calculus per urethram, urine examined found normal. Family History and habits satisfactory.

Leucocytes	Before	2	4	12
	7900	12700	12900	20800

Differential Count: /

Differential Count:	Hours after		
	Before	2	12
Polymorphs	49.6%	47.6%	82.5%
Lymphocytes	44.5%	40.8%	6.5%
Large Mononuclears	2.8%	3.4%	4.6%
Eosinophiles	.6%	5.4%	.9%
Basophiles	-	-	-
Transition Polymorphs	1.5%	2.8%	5.5%

Case XII.    Female aet 29.    Housewife.

Puerperal Septic Arthritis, 10 days after delivery. Stiff Knee resulted- occurred 2 years previously.

Leucocytes	Before	2	4	12
	19700	16400	16500	20800

Differential Count:	Hours after		
	Before	2	12
Polymorphs	43.9%	52.5%	63.6%
Lymphocytes	43.6%	39.0%	26.1%
Large Mononuclears	5.6%	3.3%	4.4%
Eosinophiles	4.6%	2.4%	2.5%
Basophiles	1.1%	1.7%	.9%
Transition Polymorphs.	1.2%	2.1%	2.5%

SERIES A./

SERIES A.

	<u>Before</u>	<u>12 hours after</u>
Case 1.	7900	22600
" 2.	7900	12700
" 3.	11800	11600
" 4.	4600	5100
" 5.	9800	22600
" 6.	4300	19500
" 7.	11800	9300
" 8.	10000	19400
" 9.	4700	9100
" 10.	9400	18600
" 11.	6300	17600
" 12	8000	18700

SERIES B.

	Before	Hours after Nucleic Acid 60 m.			
		2	4	6	12
Case 1.	7600	8200	12260	14600	14600
Case 2.	10900	7300	12200	12000	18500
Case 3.	12500	13100	3900	12100	13400
Case 4.	6300	8800	11200	11000	15500
Case 5.	7300	6400	8000	7100	7600
Case 6.	4600	6200	4600	6400	5700
Case 7.	26200	15400	11100	12400	15800
Case 8.	9600	12800	11400	17000	21000
Case 9.	13400	11800	11000	12800	4100
Case 10.	10200	5400	5500	6100	22800
Case 11.	7900	9200	10800	27500	28200
Case 12.	14200	14000	16700	15700	14800

SERIES C.

	Before	Hours after Nucleic Acid 60 m.		
		2	4	12
Case 1.	5300	5800	8300	10200
" 2.	13600	18200	22600	24200
" 3.	6800	6400	8800	12000
" 4.	14400	9100	11800	29900
" 5.	11600	8400	5100	12400
" 6.	9100	11400	11900	18400
" 7.	6100	7600	6100	13600
" 8.	9300	12600	16200	38200
" 9.	6400	6000	8000	10200
" 10.	11500	9800	9600	16600
" 11.	7900	12700	12900	20800
" 12.	19700	16400	16500	20800

In every case investigated the blood was taken from the lobe of the ear, and not from the site of injection of the Nucleic Acid.

I shall first discuss the results obtained in General Leucocytosis before considering the question of the Differential Counts or Qualitative Leucocytosis.

GENERAL LEUCOCYTOSIS:

In discussing this question one must first consider what a normal leucocytosis is, and in adhering to the opinions of Muir and von Limbeck<sup>1</sup>- that 4,000 - 10,000 constitute a normal leucocytosis, one must not forget to consider that, whereas 10,000 may be a normal leucocytosis and not out of the ordinary, in a strong and robust individual; yet the same number would be approaching that of a hyperleucocytosis perhaps in an individual whose physical stamina and constitution worn down by disease are of low standard. So therefore, in considering the cases which come under Series B. one finds that in the first instance only 2 cases (3 and 7) started with a leucocytosis. Case 7, especially, showed a hyperleucocytosis which could in no way be accounted for. Certainly Digestion Leucocytosis could have played no rôle, for if we accept Rieders<sup>2</sup> authority that the average increase is only 33% in excess of the normal figure, the 22600, which Case 7 presented at the commencement prior to injection, would not surely answer for such increase. Even if it/

it did, the prime leucocytosis would still have been high. Again: Case 2 may be looked upon as a healthy individual, whose only illness was the accident mentioned and whose wound was healing well, and in whose case 10200, was the initial leucocytosis. In the second type of cases where the individual was worn down by long standing disease (e.g. Case 8) there was a fair leucocytosis of 9600 which, in the face of widely disseminated disease may nearly be termed a hyperleucocytosis. Case 9 which had 13400 leucocytes prior to injection may certainly be placed in this category for he had been suffering from a long standing illness which had weakened him to a degree of emaciation.

In Series A. Cases 3, 7, 8, may be held as those whose leucocytes were above the normal since they were all reduced by disease of long standing.

In Series C. we have cases resembling those types as in Series B. Cases 2 and 12 may be placed in the second type. Case 2 showed Carcinoma and was much emaciated. Case 12 had a history of Septic infection.

In returning to Series A. one finds that, in 10 cases, there was an increase in the amount of leucocytosis. An increment of over 10,000 in 5 cases/

cases, and in 5 cases ranging between 400 and 9,000. The largest increase was 15,200; and in this respect the results agreed entirely with those of Hahn of Munich and Von Meyer of Prague who claim respectively to have doubled the original number of leucocytes, and to have had an average increase of over 75%. It may be urged that in Case 2. there was not a leucocytosis subsequent to the administration of Nucleic Acid, but that such leucocytosis was due to the existing Tuberculous condition. The idea, I think, may be refuted by the observations which have been made regarding leucocytosis and Tuberculosis unless there is some complication, or unless there is some cavity formation and suppuration.<sup>3</sup> In Case 2 although there was Intestinal tuberculosis there was yet no tuberculosis of the lung detected, nor did the case show any symptoms pointing to Pulmonary mischief. In only 2 cases was there any reduction and this reduction varied between 200 and 2,500. In neither case however could it be called a Leucopenia.

In discussing Series B. one has to observe two points. Firstly; whether there is much increase, or a decrease in leucocytosis at a period of 12 hours after administration of the acid. and, Secondly; whether there is decrease in the initial number during the periods at which Counts were/

were made. In considering the first point one finds that increase in number after 12 hours occurred in 10 cases. Of these, 6 cases showed a very substantial increment. One case also had its original number increased by over 20,000. Two cases gave a comparatively small response. Whilst the remaining two cases produced negative results. Diminution reached so far as from 9,000 - 12,000 of the initial number and it will be noticed that these two cases presented a hyperleucocytosis at the start. The second point to attract notice is the variation in Counts which followed the dosage. 4 cases showed a gradual increase up to the 12th hour, whereas in the remaining cases this was not so. Here there was an undulation; Increase followed by decrease which in its turn was followed by an increase, and vice-versa, or in another case, decrease followed the initial leucocytosis but was followed by a rise until the last count was taken. In these respects I am inclined to agree to some extent with Joas and Löwit who found that increase in leucocytosis was first preceded by a diminution,<sup>4</sup> but I am not prepared to say that such occurs in every case for in some cases no diminution occurred.

Now we turn to the last Series - C. In this/

this group every case showed a positive reaction at the end, and in this group also there was, on average, a more gratifying majority than in the other two groups. The maximum increase yielded 29,900, whilst the others with one exception gave increase over 1000, and in the exceptional case this figure fell short by 200 only, and even cases which commenced as leucocytosis or hyperleucocytosis yet yielded increase and did not end in decrease. In the periodic counts five cases showed a diminution after two hours but of these, four cases soon regained their position and continued to rise. The remainder sustained its deficit to the 4th hour and then rose to its maximum.

Differential Counts or Qualitative Leucocytosis:

In reviewing this portion of the subject I shall consider the question in regard to the various forms of leucocytes and shall not discuss them separately under the three series. Whilst doing so I shall mention what was found concerning the peculiar appearances in size etc., of the various leucocytes.

I./

I. Polymorphonuclears or Polymorphs.

The increase of this form of leucocytes ranged between 5 per cent and 38 per cent. A decrease of 6.2 per cent was observed in one case. The lowest percentage observed prior to the administration of Nucleic Acid was 29.8, and the highest percentage observed was 77.5, although this, the highest, was followed closely upon in another case by one of 76.3. In this latter case only 9600 leucocytosis was present. One should draw attention to the fact that in Carcinoma cases it is not always the rule, as is suggested by Da Costa,<sup>5</sup> that Polymorphs are below the normal percentage. On the other hand, a comparatively high percentage was observed, in such cases, on more than one occasion. It was also found that as leucocytosis advanced, for example in Case 4 of Series B. the tendency of the Polymorph percentage was also towards increase, but this again was not absolutely the rule; for in those cases where two hourly counts were taken, although the leucocyte count increased, nevertheless there was rather a decreased percentage of Polymorphs. Nor did the converse hold. In addition, a diminution in percentage of Polymorphs did not imply an increased percentage in lymphocytes. On the whole however, where there was a hyperleucocytosis at the 12 hour period/

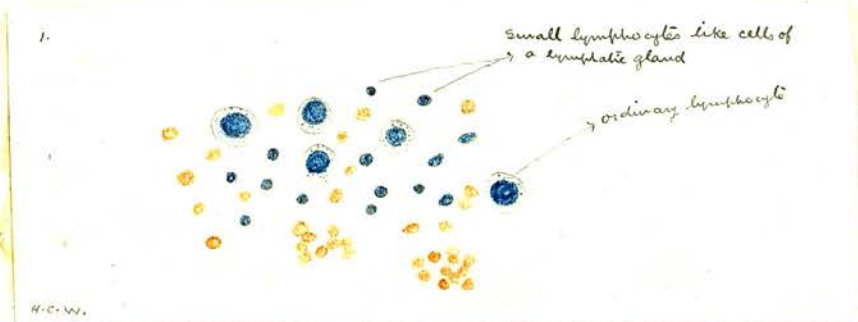
period there was also a high percentage of the Polymorphs, - reaching up to 84.4 in one case and 81.3 in another. In cases which received 20 minim dosage the increased percentage was higher than in those whose dose was 60 minims. Taking all the series into account it was found that, at the 12th hourly count, whether there was increase or decrease in leucocytosis, the Polymorphs showed a relative increase in percentage, markedly so in some instances. In other words; the blood obtained after 12 hours was rich in Polymorphonuclear leucocytes.

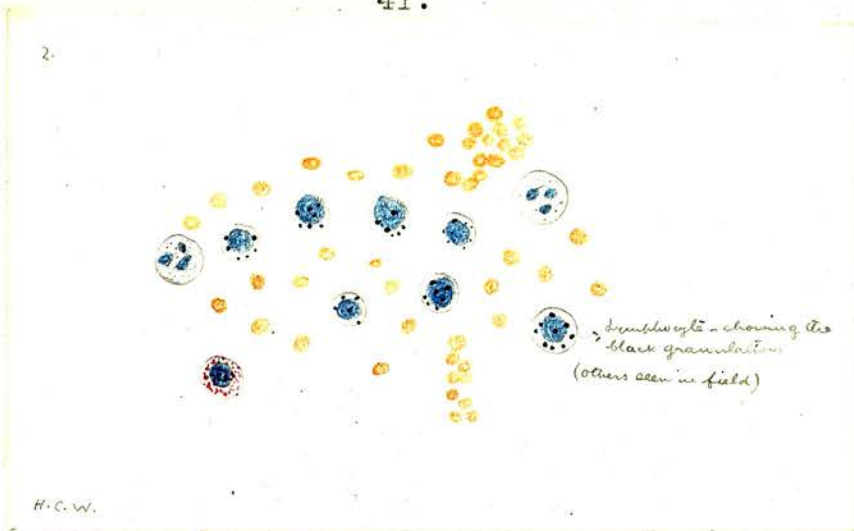
In commenting on the size of the Polymorphs it was observed that they varied in size. The general tendency was that they were of their normal shape and size before the Nucleic Acid was administered, but during the periods after administration they often showed a diminution in size and their size in many cases did not exceed that of the small lymphocytes. In defence of this statement it must be urged that great care was taken in examining them closely in order that a deceptive mistake would not be made in describing an amoeboid lymphocyte as a Polymorph.

II./

## II. Lymphocytes:

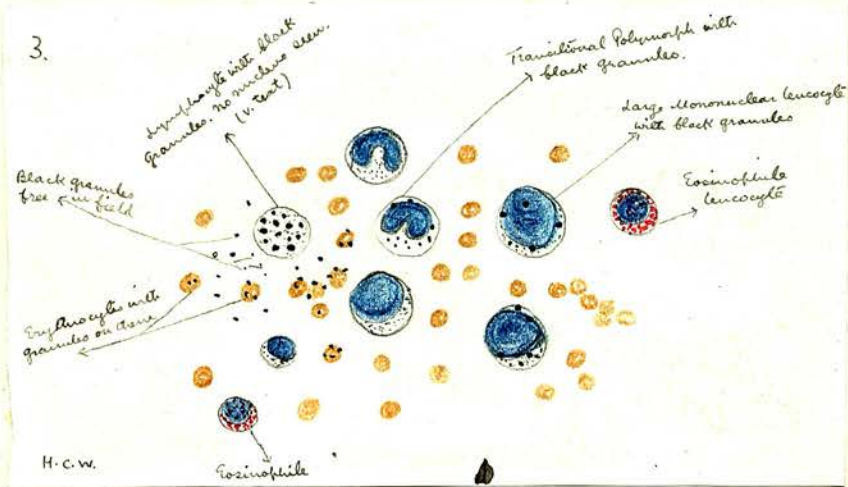
The lymphocytes varied between 62 per cent, and 9.9 per cent, and here again, if the normal percentage is to be accepted as comprising 20 - 30 per cent, the above numbers 62 and 9.9 have shown a great variation. The commonest occurrence was for the lymphocytes to diminish in percentage from the commencement, towards the end of the counting periods; and their increase and diminution to vary inversely with the increase and diminution of the Polymorphs. These observations agree with those made by authorities on leucocytosis who assert that such takes place. The lymphocytes varied in size, some being of the normal size, whilst others were much smaller, and their appearance on slides were like unto cells of lymphatic glands; and it is very conceivable that they were, from the "impulse" given to the increase in leucocytosis, forced to enter the circulation in their immature condition. They were not present in those cases which had no appreciably increased leucocytosis.





Another remarkable phenomenon was observed in the appearance of the lymphocytes, and this was the presence, in some of them of peculiar black granules arrayed in perinuclear fashion, and in some instances over the nucleus. This condition was present in 10 cases. The granules were of an intense black colour. Some were coarser than others. They were not abundant enough to obscure the nucleus of the cells in which they were present. But in one particular instance they were present in a lymphocyte and were of the coarse type. This lymphocyte was lying amongst other lymphocytes and although the latter were clearly stained, this solitary lymphocyte

appeared unstained and even its nucleus was not to be distinguished, its place seeming to be replaced by the black granules. The lymphocyte in other words appeared to be in a state of disintegration. In one slide fine black granules were seen scattered freely about a few leucocytes and it is probable that they were derived from cells which had, during disintegration, contained them, but which (cells) after utter disintegration and dissolution had set them free. In one instance some erythrocytes appeared to be impregnated with these granules but one is inclined to consider that the granules were lying on them, by mere accident, and were not contained by them.



It is possible that, admitting the nucleus to be the most essential part of the cell, these granules were derived from, and indicated a Katabolic process/

process of, the nucleus; since in the lymphocyte already cited the nucleus was not visible but its place taken by the black granules.

Now although the above theory may explain the presence of these granules, yet the cause of their presence is not explained. Neusser,<sup>6</sup> despite strenuous opposition offered, has asserted that he found these granules in leucocytes in the blood of those suffering from Gout, and that they indicate a Uric Acid diathesis. Other observers have found them in the blood of those suffering from Chronic Tuberculosis, Diabetes, and Myelogenous Leukaemia; whilst Pascheles<sup>7</sup> is convinced that they indicate no diathesis at all. If, as we are told, these granules are, of a chemical nature, allied to Nucleo-albumin, then it is very probable that Nucleic Acid, so closely allied to Nucleo-albumin, is in itself greatly responsible for such changes, and that its influence is exerted, to some extent, towards destruction of the white Blood Corpuscles. In defence of this assertion it may be urged that the appearance of these granules coincided with the periods where there was a reduction in number of leucocytes, either following a leucocytosis, or following the count taken prior to the giving of Nucleic/

Nucleic Acid. Although this view cannot be considered as absolutely tenable since it occurred in two cases which had a Chronic Tuberculous disease, and prior to administration, yet as it occurred in other cases which were not afflicted with any of the diseases above mentioned, the action of Nucleic Acid goes far to explain the phenomenon.

### III. Large Mononuclear Leucocytes.

This type of leucocyte, in its percentage increase or decrease, bore no relationship to the increase or decrease of the other leucocytes. It was found, that in cases having chronic disease and showing emaciation, their percentage was increased above the normal. In one case of Carcinoma the percentage reached as high as 18.7 twelve hours after injection of Nucleic Acid; thus giving an increase of 12.1 per cent on that taken before injection. In one case six hours after administration some mononuclears were seen with black granules present in the cytoplasm and about the nucleus; but none of these leucocytes appeared to be in a condition of complete disintegration.

### IV. Transitional Polymorphs:

These were found in one instance to have reached as high as 8 per cent, but they did not show any/

any special increase or decrease in any particular type of disease. It was observed however, in many instances that, where there was a rise in the tide of leucocytosis, it was difficult to discriminate between a Transitional Polymorph and a Polymorph. In the same case where the black granules were seen in the Mononuclear Leucocytes the same phenomenon was observed also in a Transitional Polymorph.

#### V. Eosinophile Leucocytes:

were present in two forms:- Small leucocytes with fine red granules, and larger leucocytes with coarser granules. The former type was more frequently present than the latter. In cases which received dosage of 60 minims the Eosinophiles were more abundant prior to injection than at any other period. But in cases to which 20 minim doses were administered the Eosinophiles were most plentiful 2 hours after the administration. Only in one case which had Carcinoma was there a high percentage of 6.1. This percentage was not sustained throughout after Nucleic Acid was given but it soon fell. Nucleic Acid seemed to have a repellent rather than an attractive influence on the Eosinophile leucocytes, and especially when given in doses/

doses of 60 minims.

#### VI. Basophile Leucocytes.

If .5 is to be considered as the maximum percentage of Basophiles in a normal leucocyte counts, then 2.5 per cent may be taken as a degree of Basophilia, which condition was found in only one case and this was one of malignant disease. This degree of Basophilia persisted throughout the periods in which blood counts were taken and was not influenced by Nucleic Acid.

Nucleic Acid seemed to have no action on the Basophile leucocytes in any way for they were as often absent as they were present.

#### Effect of Nucleic Acid administration on Temperature, and on Local Disturbance and "well-being" of the cases under investigation.

##### (a) Temperature:

In order to determine whether the temperature was influenced in any way by Nucleic Acid injection it was taken in every case before, and 12 hours after the acid was injected. In 36 cases under investigation, 23 gave a positive reaction, 10 showed a/  
a/

a diminution; whilst in the remaining 3 cases there was no change in temperature. Of the 23 cases which gave a positive reaction 12 were of Series C. It was observed that, in Series A. and B., increase of leucocytosis was not necessarily attended by increase in temperature. But in Series C. all the cases or 100 per cent responded to increase of leucocytosis with an increase in temperature. Increase of temperature generally ranged between  $.4^{\circ}$  and  $3.2^{\circ}$ . In no case did a hyperpyrexia occur.

(b). Local Disturbance and well-being etc:

In every case there were tenderness and a little pain experienced at the side of injection, but these were not of themselves enough to prevent sleep between the intervals at which counts were taken. In some cases a feeling of stiffness in the limb was complained of but this was often transient. No giddiness, headache nor any other general discomfort were otherwise met with, and the action so far as disturbance was met with was soon forgotten. Only in two cases did the area around the site of injection become firm to the touch and reddened; but this only persisted for two days at the most. Relief was obtained by hot Boric fomentations. No suppuration ensued.

The/

The nature of Leucocytosis with Nucleic Acid. How  
is it brought about?

Some authorities as Ehrlich, Muir, Goldscheider and Jakob agree on the question of chemiotaxis as being the way and means in which Nucleic Acid exerts itself on Leucocytosis. Joas and Lowit on the other side are unable to accept this view and consider that leucocytosis is an act of regeneration. Whereas Schultz<sup>8</sup>, who experimented on rabbits, obtained negative results and considered increase or decrease due to unequal distribution of the white cells in the circulation. It seems difficult at first sight to understand why leucocytosis should occur, as Joas and Löwit think,<sup>9</sup> and not continue to do so throughout the periodic counts. But if the theory be accepted that the "Black Granular" leucocytes betray a condition of commencing disintegration and that this would continue to take place until the acid (Nucleic) was reduced to a certain strength by elimination so as not to produce any further toxic action, then the view as held by Joas and Lowit is not so incomprehensible after all. Certainly; in comparing the results obtained in Series B. and C., it will be found that the majority of cases, which revealed/

revealed a diminution following increase, occurred in Series B. where the dose was stronger than in Series C. This would tend to favour the view that there might be a greater leucolytic change after a dose stronger than 20 minims, and a less leucolytic change after doses smaller than 20 minims. The Regeneration process might be explained by leucocytes being sent into the circulation to fill up the gap left by destruction of the preceding ones. This would occur if the reparative powers of the individual were sustained and not exhausted - when a leucocytosis or a hyperleucocytosis would ensue, but would fail if the leucoblastic structures were broken down, so to speak, as in great degrees of emaciation, ending in a progressive and confirmed leucopenia.

As it was not easy at first to accept the leucolytic theory, still less so is it to accept the theory of the influence by Chemiotaxis "per se." If there is to be a positive and a negative chemiotatic action, then surely there must be some change going on somewhere to explain a diminution at one period and an increase at another. This change would have to be located in places where the leucocytes are formed, as in the bone marrow and lymphatic/

lymphatic glands. It has been shown that arrangements in the marrow are such as to bring the leucocytes in it directly under the influence of any substance circulating in the blood, and, at the same time are such as to admit their ready passage from the marrow to the blood. This would help to explain the increase and not diminution, and the problem of the repellent action (of Nucleic Acid) would still remain to be solved. If a pure and simple, and not a toxic repellent action occurs, the question next to be asked would be, where does the repulsion take place? Is it from the peripheral circulation to the central? or vice-versa? To ascertain this would require methods to enable comparisons being made between a central and a peripheral leucocytosis at the same time.

CONCLUSIONS:-

Having surveyed the results obtained from my experiments and investigations, and having attempted to promote arguments which have followed in the train, either in one favour or in the other, I shall now proceed to make deductions and to draw conclusions from what I obtained. These deductions and conclusions will be appended as follows:-

1. Nucleic Acid 5% solution, obtained from yeast, tends to produce leucocytosis in varying degrees. Variations depending upon the time, and the amount administered.
2. The most favourable time for studying its effect upon leucocytosis is at night, for then the tendencies to error, in holding leucocytic increase, due to Digestive processes, which during the night are not so active, and to other agents and factors, etc., are greatly minimised.
3. Leucocytosis is not progressive in every case. There may be an increase preceded by a diminution and followed again by an increase. This occurs especially when 60 minim doses are employed rather than when 20 minim doses are used./

used.

4. The Maximal Leucocytosis was found to be generally 12 hours after administration, and this was always the case when 20 minims were employed.
5. The period at which the effect of Nucleic Acid was at its height was 12 hours after administration for then the Polymorphs, which are essential for phagocytosis were, of all the various leucocytes, most increased, even out of relation to general leucocytic increase.
6. As the repelland action, which is of a toxic nature, was found to be commoner with a 60 minim dosage, it is better to give smaller doses as 20 minims which tend to give higher results.
7. In cases where there is a leucopenia preceding injection, it is very questionable whether this will be improved upon by administration of Nucleic Acid if there is reason to believe that the leucopenia is due to exhaustion of the blood forming apparatus. Nucleic Acid would tend rather to/

to cause further depression without any corresponding benefit of increase.

8. Nucleic Acid has no effect in increasing the production of Eosinophile leucocytes. Should such increase be desired for disease e.g. Pneumonia where the production of Eosinophilia might forebode a hopeful prognosis, should this be very dismal, the effect of administering the acid for this end would be only futile.
  9. Increase of leucocytosis is generally attended with increased temperature, varying between a decimal increase and 2-3 degrees.
  10. Little disturbance - general or local, follows administration of the drug.
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