CUTANEOUS MANIFESTATIONS

	Hypo State	Hyper State	Remarks.
Pigmentation Yellow to bronzing	(Addisons (Chronic		Not produced in experimental animals. Not lessened by any known therapy. In the Addisonian, may be transcent in other type. (produced in one of our animals by taking off lymphatic duct.
		Cortical Tumor	One of secondary manifestations of cortical tumors of sex stimulating type during stage of hypo function. Disappears slowly after removal of tumor.
Pseudo anemia	Low functioning adrenal, seen in pampered children and		Normal pink color can be secured by adequate doses of cortical extract. test cases are usually sensitive to sun and do not tan, but after cortin therapy, tan as well as others.
Urticaria	(Addison (Hypo-function		Seen in the Addisonian and in hypo-adrenal states similar to sensitivity to drugs, insulin, toxins, etc.
Excessive and odorous perspiration	Hypo states		A cutaneous manifestation of nervous origin. Possibly due to lack of capillary tone of deep structure; rectified by adequate salt intake with or without appropriate glandular therapy.
Conjunctivitis	Addison Hypo states		In the patient with Addison's relieved by cortin and adequate salt intake. In hypo states usually accompanied by hay fever; similar therapy.
Eczema and other skin lesions, psoriasis	?		Recent report from Canada recommends use of epinephrine ointment to blanch skin, & soften skin, in conjunction with calamine, etc. Report from Germany recommends use of cortical substance systematically. Independently of these reports, we have used the combination of epinephrine ointment in petrolatum base and cortical substance by mouth.

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Cutaneous manifestation of cardio-vascular origin.

	Hypo state	hyper state	
Cyanosis	hypo state		Insufficient oxidation and circulatory rate. Epinephrine and saline intravenously.
Purpura	Usually accompanies adrenal		Most remedial measures are usually of no avail as condition is more often bilateral or due to hemorrhagic cysts; supports treatment only. However, may be seen in hypo states supposedly due to loss of capillary tone.
Gangreen - angiospastic		Thrombo angitis obliteran	Supposed to be due to prolonged medulary hyper function Hypertrophy of muscular coat of vessels and contraction; relieved by unilateral suprarenalectomy and sympathectomy.
		Transient angiospastic	Usually due to medulary tumor. treatment, sympathectomy.
		Hypodermic of epinephrine	Epinephrine given in doses of 1-10,000 and less will sometimes cause necrosis and sloughs
&			
Cardio Vascular. Faint Heart sounds Small heart muscle Low Bloos pressure Palpitation Tachycardia Dispnoea (cardiac Vertigo Fainting attach Chilliness	Addison's disease. Amyloidosis of adrenals. Metastatic tumor of Sclerosis of adrenals/ Other hypo states		These are cardial symptoms of Addison's disease and are seen in the other hypoadrenal states mentioned. There are a result of lowered oxidation rate causing a general hypotonia with the attendent lowering of the circulatory volume and rate. Blood pressure is usually low-60/100 but may be over 140. To compensate for low volume, tachycardia is frequently present but the stroke seems ineffectual. Treatment, cortin and salt.
Shock	Acute episode		Many of the above can be classified as shock symptoms such as low blood pressure, tachycardia. This is seen in many conditions. It is usually transient. Epinephrine by intravenous route in saline, 1-50,000 or 1-100,00.

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Cutaneous manifestations of cardio-vascular origin.

	Hypo state	Hyper state
ecxema and other skin		

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Cardio-vascular, Continued.

Splanchnic dilitation	Hypo states		Usually accompanied by pale alabaster skin condition frequently chronic. Cortin and salt.
Hypertension Low Blood Value		Medulary over-function or tumor	Attacks may be noted of transient character lasting from 2 minutes to several hours accompanied by tachycardia, feeling of constriction, fear, loss of and transientglycosuria, without necessary blood sugar use. Attacks may be continuous with blood pressure up to 300 mm. hg. Treatment: removel of tumor or partial cortex adrenalectomy.
BIO Chemical			
Loss of no concentration of blood	(Experimental. (Addison's (Hypo States		Loss noted in both totally adrenalectomized animal and Addison's disease and other hypo-states. If entire cortinal adrenal function is not distroyed adequate sodium chloride intake may be sufficient. In total destruction use of cortin is augmented by Sodium Chloride intake.
Loss of Cl_5HCO_3	(Experimental (Addison's (Hypo states		Same as above.
Increase of	(Experimental and Addisons		Some have postulated that the effect is to a degree responsible forthe cardiac disturbance. It decreases to normal with cortin therapy augmented by adequate sodium chloride intake.

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Bio-Chemical Con't

	Hypo	Hyper	Remarks and treatment
Increase in non-protein nitrogen	Experimental and Addisons		non-protein nigrogen figures may be as much as ten times the normal in dogs dieing from adrenal insufficiency, and reach very high levels in the Addisonian.
Decrease in blood sugar	Experimental, Addison and Hypo states		Accompanied usually by low rise in tolerance.
Glycosuria		Medullary, hyperfunction and tumor	May be permanent but is usually transient Suprarenalectomy or removal of tumor.
Loss of Plasmo volume	Addisons, Amyloid degeneration. Experimental animals.		Loss due to increase in urination at initial period of insufficiency. Quickly improved by cortin and salt.
Basal O_2 consumption	Experimental. Addisons Amyloid & hypofunction.		Lowered basal rate may not appear until late in Addison's disease or hypo states. It may be compensated for by other ways in amyloid degeneration. In the suprarenalectomized animal, it drops rapidly after the 4th day. Corrective measures, cortin and salt.
		Hyperfunction of medulla or tumor.	Causes increase in b.m.r. It may be temporary and recurrant or may be fairly constant simulating thyroid disease. Removal of tumor or unilateral suprarenalectomy & sympathectomy.
Increase in plasma protein	Experimental Addisons Hypofunction states		Increase in elements too is noted as well. Relieved to normal by cortin.
Blood lipins	Addisons		Sometimes slightly increase.

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Bio Chemical

	Hypo	Hyper	Remarks and treatment
Anemia	Addisons Hypostates	Hyperfunction of Medulla	Anemia in these cases is rare, contrary to Addison's first description; however in states of hyperfunction of the medula, a secondary anemia that readily responds to massive iron dosage is present.
Creatineuria	Addisons Experimental		A terminal condition seldom benefitted by therapy.
Gastro-intestinal symptoms			
Constipation Diarrhoea Hypertonia Hyperchlorhydria Hypochlorhydria Atonia Achylia Peptic Ulcers Duodenal ulcers Pseudo angina Anorexia Nausea Vomiting Belching Tympanitis Epigastric pain Emaciation Relaxation of Muscles	Addisons Suprarenalectomy Hypo states		Constipation is the rule in the Addisonian, but in terminal cases there may be a diarrhoea. This constipation is frequently seen in hypo states and can be adequately taken care of by the adminstration of sodium Chloride. In the Addisonian salt may or may not be sufficient, but the addition of Cortin quiets the condition. In the early stages of the disease, hypertonia is present with a hyperchlochydria and a spastic colon and a hypermotility of the small bowel, and stomach. During this period there is frequently reported an insatiable appetite. Finally this passes into a hypochlorhydria and hypo tonus, spasticity of the colon, passing off more gradually, and finally achlorhydria or atonia with the attendant constipation which at times even sodium chloride and cortin require aid from posterior pituitary extracts. In the early stages nausea is frequently present with tympanitis and belching symptoms which progress with the disease. Early peptic and duodenal ulcers may be seen less

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Gastro-intestinal con'd	Hypo	Hyper	
			frequently in the middle or terminal stages when the pseudo peritonitis symptoms are more prone to occur. Here frequently cases have been operated on for supposed ontra abdominal pathology, most frequently appendicitis, for the pain is usually primarily epigastric. Hiccough too may be present with the condition making an extensive peritonitis seem real. Rigidity of the abdominal musculature may or may not be present in these apisodes. The hiccough too may be a prominent symptom of damage due to acute toxic processes or adrenal hemorrhage. In the atonic stage of the disease actual shrinking of the oesophagus, stomach and intestinal tract has been reported. In this stage anorexia is always present and nausea and vomiting, not forceful but more of a drooling becomes a prominant part of the gastro-intestinal picture.
	Hemorrhage Toxic		
		Hyper-cortical	In the cortical tumors there is some times a diarrhea with an increased demand for food. If however the tumor progresses the typical symptoms of the Addisonian set in. Removal of the tumor is the only remedy.
		Hyper-medulary	In the hyper medulary type of tumor actual spasms of the intestine may set in at the time of attack. This is characterized by left apigastric pain. During this period, anorexia is present. These patients are usually severely constipated.
Vomiting of pregnancy	?		This condition can be relieved in many instances by cortical extract and salt, therefore adrenal damage has been postulated as a possible cause.

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Gastro-intestinal Con'td	hypo	hyper	
Gastric cramp		injection of epinephrine	1/16 gr. of epinephrine when injected on an empty stomach frequently produces severe gastric cramps. This cramp starts in the upper left quadrant and radiates down toward the umbilicus and lower right quadrant. According to S. Levy Simpson it is a contraction of the jejunum.
		cortical	The ingestion of cortical material on an empty stomach also causes a gastric cramp. This cramp however seems to be located more in the right upper quadrant. Both are extremely severe. When whole raw glands are ingested the cramps are so severe, and generalized throughout the abdomen, that it is very difficult to locate any single pain. The cortical pains can be induced by intravenous administration of cortin. Nausea and vomiting sometimes follow the use of the oral administration of the cortical extract. The gastric cramp can be avoided by giving a diet rich in non-precipitated hydrophilic colloids such as raw meat, gelatin, milk, etc. Carbohydrates, fruit juices etc., augment the pain.
Apetite	X	X	Patients placed on cortical extract for hypoadrenal states frequently report a marked increase in appetite with resultant gain in weight. This however, is followed by a lessened demand over their normal for food, still maintaining or gradually increasing their weight.

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Genito Urinary

	hypo	hyper	
Loss of libido Impotence	Addison Hypo states	Hyper states	Loss of libido and impotence may be present early or late in the Addisonian. It usually develops late in cortical tumors. In assumed hypo states the administration of cortical extracts and whole raw gland (this fraction is possibly separate from the life sustaining principle) has to our knowledge resulted in pregnancies in 5 cases where there had long been sterility and no contraceptive measures had been followed.
Shift in puberty	hypo	hyper Cortical tumor	In hypo states puberty is sometimes delayed. It is possible that cortical extracts may help bring on delayed start of menstruation in girls. We have a suggestive case in our records. On the other hand, cortical tumors have been responsible for precocous puberty as early as 5 years.
Pseudohermaphrodites mascularising female feminizing male Homosexual precosity male and female Heterosexual precosity in female		cortical tumors	The disturbance of sex characteristics caused by cortical tumors depends somewhat on the time the abnormal growth sets in. If it is congenital in origin, it is sometimes almost impossible to tell the sex of an infant. Male children may apparently have the external genitalia of the female and vice versa. If it develops in childhood, in the male the infantt Hercules type is a result. In the female menstruation may begin as early as 5 years. Tumors later on in life are far more frequently found in the female. Here the woman grows a beard. She first of all has great energy, which gradually passes off and if not treated may develop the Addisonian symdrone. Besides the phenomenon of hypertrichosis, she developes a masculine voice and general features change to the male type. In the male, the changes are less predominant,

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Genito-urinary con'td	hypo	hyper	
			being unusual growth of hair over body, increase of strength at first gradually going away. Surgical removal of the tumor when possible is the only treatment of these cases. They are usually benign growths but may be carcinomatous. Early in the development of these tumors, either male or female may have tremendous increase of libido.
Loss of menstruation	Addison Amyloid	Cortical tumors	Menstruation loss is frequently seen in chronic tuberculosis where amyloid degeneration sets in. It also develops in Addison's disease and in diseases of the cortical tumors. In the first two, cortical extract aids in bringing a return of the functions. In the latter, removal of the tumor is sometimes effective.
Change in menstrual cycle and painful menstruation	?		In some cases of postulated hypo states where there has been profuse bleeding, pain or irregularity we have given the cortical extract or cortical extract and epinephrine by mouth. The epinephrine is given to relieve the menstrual cramp while the cortical fraction to regulate. Here we may see two things, shortening of duration to 3 or 4 days with normal flow, or a lessening of the menstrual cycle to 21 to 26 days.

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Genito-urinary Con'td

	hypo	hyper	
Polyuria	experimental		Polyuria follows second suprarenalectomy; this state is also noted in withdrawing cortical extracts when treating cases of supposed adrenal hypo function.
Abortion Absence of lactation Degeneration of testes Atrophy of seminal vesicles Atrophy of ovaries Atrophic changes in pituitary	Addison's Suprarenal		The reproductive functions are disturbed in Addison's disease. On adequate therapy (cortin) these functions partially return to normal, provided the condition has not existed long enough to cause complete degeneration of function of part of the organs involved. In states of assumed hypoadrenia, fertility has resulted from adequate cortical therapy in previously barren subjects.
Hematuria		medulary tumor	In certain cases of apparent adrenal tissue found in the kidney, small cysts develop, causing extravacuation of blood and hematuria. This condition may precede a malignant hypernephrona supposedly of adrenal origin.
Pain in Back	Addison's Hypoadrenia	Cortical & medulary tumors	Pain in the back is a fairly constant accompaniment of all adrenal disfunction. It has sent female patients with Addison's disease to the opating table and in hypo cases with their accompanied menstrual disturbance adequate cortical therapy relieves the hypo states, while surgery cars fpr the other.

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NEUROLOGICAL SYMPTOMS

	hypo	hyper	
Mental asthenia Poor concentration Irritability Nervousness Anxiety Personality change Insomnia Depression Mental prostration Delerium Coma	Addison's Amyloid Hypo states		As the Addisonian develops his mental symptoms, they may first be noted as an increased irritability with lack of concentration. As it develops he becomes very restless, his personality changes from one of cheerfulness to one of despair. He suffers from insomnia. Becomes very dull and may develop psychosis of persecution . He becomes very iatrospective; as his disease continues he enters into a state of mental prostration where even thought is an effort and he may lie for hours in a daze. As the condition becomes terminal, a period of muttering delerium sets in, finally coma, and death.
Mental alertness increased sociability Personality change fearlessness increased ability to concentrate General feeling of well being Increased ability to sleep.		hyper	In contrast to the above is the effect of feeding 5 gms. of whole raw adrenal to normal subjects. Besides its physical energizing properties, it also is a neuro psychic energizer. Ther personality change is toward extraversion; there is great desire for work; efforts of all kinds are easier. One breathes freer and feels as though the world were his.
Spinal cord degeneration	Addison's		In cases of long standing Addison's disease, degeneration of the lateral and pyramidal tracts may set in; once established, no therapy is effective.
Neuro-muscular pain	Addison's Hypoadrenia		The neuritis of the Addisonian is frequently very painful. Likewise it is seen in cases of amyloidosis; chronic illness, such as cancer, arthritis, tuberculosis etc., active cortical extracts and those such as the Coffey-Humber not active in life giving principle, give relief from certain of these painful epidodes.

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Neuropsychractic Aspects

	hypo	hyper	
			Severe pain in extremities may be forerunner of oncoming Bergers disease with its intermittant claudication; here lateral supprarenalectomy and sympathectomy is the treatment.
Hyerthesia and hypothesia	Addison's		The addisonian on occasion presents areas of hyper and hypothesia. These are usually accompanied by spinal cord changes. This pain is allayed by cortical treatment, but underlying pathology is not aided.

RESPIRATORY SYMPTOMS

Hoarseness Pain on speech Choking sensation Costo-vertebral tenderness Asthma pulmonary despnoea Shallow respiration Rapid respiration Bronchial ronchi Chronic bronchitis Constriction of chest Susceptibility to pneumonia and respiratory infection	Addison's Supprarenalectomy		Although gastric, genitourinary, neuropsychiactric, and general symptoms of Addison's disease are freely discussed by various writers little stress is laid on the pulmonary side of the disease.; except by the experimenters who find that pneumonia and lack of resistance to respiratory infections is their most serious problem in preserving their animals. The above tabulation is therefore gleaned more from reported histories rather than the writing of others.
Colds		X	There the adrenalectomized animal is more sensitive to respiratory infections than usual, we have found that adequate dosage of cortical hormone orally and by hypodermic injection will frequently abort colds in the early stages. If however, they have set in the toxic symptoms are largely relieved and the duration lessened. In true influenza the post influenzal drag is eliminated

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Respiratory con'td	hypo	hyper	
Yawning stretching Gasping for air Air hunger	Addison's hypo states amyloidosis		Yawning, stretching, gasping for air etc., are all symptoms of lack of proper gaseous interchange and are frequently seen in Addison's disease. They Disappear under cortical therapy.
Relief of cough loose sputum Broncho spasm	X		Oral administration of epinephrine on a full stomach acts as an excellent broncho-sedative. The effect is prolonged. Broncho spasms apparently relaxes. Sputum becomes more watery and is easily expectorated. The effect of single dose usually lasts till the next meal. Only in the most severe cases do extra doses have to be given.
Asthma	?		This is also effective in asthma even in cases when by hypodermic injection, reversal of effect have been obtained. However, in conjunction with the cortical fraction, it is far more effective. In the asthmatic too it apparently helps to control the fundamental bronchitis and the emphysema seems to be rapidly lessened. In severe asthmatic children of 2 to 10 years standing, whom no other relief measures seem to have helped, apparently gradually lose their emphysema and bronchitis.

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