

5IF 4DJFODF BOE "SU PG 0CFTJUZ

\$ULH@6UHV

0DULH)UDQFH %RG\OLQH ,QW\O 3KLOLSSLQHV
 &RUUHVSRQGLQJ \$UDM\O 6R7RUUHV 0HGLFDO 'RFWRU 0DULH)UDQFH %RG\OLQH ,QW\O 3KLOLSSLQHV 7HO
 5HFHLYHG 2FWRUHU \$FFHSWHG GDWH 2FWREHU 2FWREHU 2FWREHU 2FWREHU 2FWREHU 2FWREHU
 &RSULJKW < 7RUUHV \$6 7KLV LV DQ RSHQ DFFHVV DUWLFOH GLVWULEXWHG XQGHU WKH WHUPV RI V
 GLVWULEXWLRQ DQG UHSURGXFWRQ LQ DQ\ PHGLXP SURYLGHG WKH RULJLQDO DXWKRU DQG VRXUFH D

\$EVWUDFW

,QWURGXFWRQ KDYH EHHQ VR PDQ\ DGYDQFHV LQ WKH ILHOG RI 2EHVLW\ ,W L
 LQWURGXFH WR RWKHU KHDOWK SURIHVVLRQDOV DERXW WKH ODWHVW LQ VFLHQFH
 D JOLPSVH RQ WKH DUW RI REHVLW\ PDQDJPHQW \$W WKH VDPH WLPH WKLW DU
 QXWULWLRQ DQG ZHLJKW ORVV RQ WKH FXUUHQW DFFHSWHG GHILQLWLRQV GLIHH
 DQDWRP\ DV ZHOO DV SK\VLRORJ\ RI IDW KRUPRQH RU DGLSRNLQH DQG UHYLH
 \$TV LQ WUHDWLQJ RYHUZHLJKW SDWLHQWV VXIIHULQJ IURP REHVLW\

0HWKRGRORJ\ REHVLW\ LQIRUPDWLRQ ZDV EURNHQ GRZQ LQWR VFLHQFH DQG DUW
 NQRZOHGJH WKDW KDYH EHHQ HVWDEOLVKHG E\ GLVFRYHULHV WKUX WKH \HDUV Z
 REHVLW\ LV FODVVILHG DQG HYHQWXDOO\ PDQDJHG

5HVXOWV 7KH VFLHQFH RI REHVLW\ NQRZOHGJH GHDOV ZLWK WKH DQDWRP\ DQG
 LQFOXGLQJ WKH W\SH RI IDW WKDW WKH\ RULJLQDWH IURP YLVFHUO VXEFXV
 GLIHHUHQWLDWH WKRWH WKDW DUH EHQHILFLDO IURP GHWULPHQWDO 7KH DUW RI
 ZHLJKW ORVV ZHLJKW PDLQWHDQFH ZHLJKW UHJDLO UHFLGLYLV DQG UHERXQ
 DGLSRNLW\ DQG WKHLU GLIHHUHQW FODVVILFDWLRQV EDVHG RQ WKH ERG\ PDVV
 FRXQWULHV XVH WKHP DQG LWV KLVWRU\ LQ WKH ,&' &XOPLQDWLRQ LV WKH
 H[DPSOHV

&RQFOXVLRQ \$GLSRNLQH RULJLQDWH IURP IDW FHOOV DIWHU WLVVXH PDFURSK
 WRR PDQ\ 7KRVH WKDW RULJLQDWH IURP YLVFHUO IDW GHHS IDW DQG XSSHU R
 RULJLQDWH IURP VXEFXWDQHRXV IDW VXSHUFLDO IDW DQG ORZHU REHVLW\ W
 PDLQWDLQH IRU D \HDU IRU LW WR EH FRQVLGHUHG VXEFXVVIXO ZLWK ORQJ WHU
 IDW DOO RYHU WKDW LW DOUHDG\ LQFUHDVHV ULVN RI GLVHDVH EDVHG RQ KHDOW
 %0,! NJ DQG D ODUJH ZDLVW FLUFXPIHUHQFH EDVHG RQ JHQGHU DQG GLIHHUHQW
 DUH DVN DVVHVV DGYLVH DJUHH DQG DVVLVW

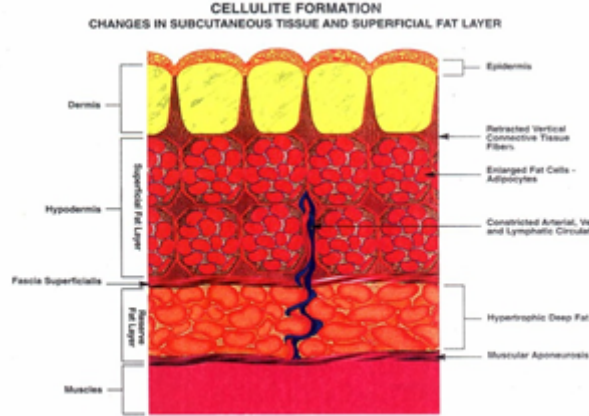
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 K\SHUSODVLD :HLJKW ORVV \$GLSRNLW\ YHUVXV REHVLW\ 4XHOHW LQGH\ RU
 ERG\ PDVV LQGH\ +HDOWK ULVN IDFWRU : LWK HDFK REHVLW\ FRQYHQWLRQ EHLQJ
 DQG SXEOLVKH\GLHV EHLQJ UHGD GDI
 PFK GDWD KDV DFFXPXODWHG ,QIRUPDV
 DYDLODEOH WR WKH DXWKRU EXW ZDV QH
 ,QWURGXFWRQ
 ,QWURGXFWRQ D\UUV DJR\WKW LQJ RI WKH REMHFWLQJ JULHV RQ WKH VFLHQFH
 DWRFLDWLRQ ZDV KMDGXDG\HQW VDWLGHSHQW IRFXVHQZ RQ WKH DUW
 REHVLW\ %\ WKH dv UHVHDFK RQ LQFUHDV\ REHVLW\ NORZOHGJH DQG
 PHHWLQJV WR HVWDEOLVK REHVLW\ DQDWRP\ DQDWRP\ GHDOV ZLWK H[DFW N
 WPH WKHUH KDYH EHHQ YROXREHGLW\ DQDWRP\ E\ GLVFRYHULHV WKUX WKH
 REMHFWLYH RI WKLW DUWLFOH WR LQWURGXJWRWKH REMHFWLQJ JULHV RQ WKH VFLHQFH
 WKH ODWHVW LQ VFLHQFH UHJDUGLQJ REHVLW\ NORZOHGJH ZRQFVWRGLVW
 JOLPSVH RQ WKH DUW RI REHVLW\ PDQDJPHQW \$W WKH VDPH WLPH WKLW DU
 DUWLFOH LQWHQGV YROXREHGLW\ WKH DQDWRP\ ZHLJKW ORVV
 RQ WKH FXUUHQW DFFHSWHG W\SH RI IDW KRUPRQH RU DGLSRNLQH V\HMSKRGV\ISHUWURSKI\ DQG
 IDWRUV FDXVDOLW\ LQ DQDWRP\ DV ZHOO DV SK\VLRORJ\ RI IDW KRUPRQH RU
 DGLSRNLQH DQG UHYLHZ VVHS E\ VVHS WKH XQLYHUVDOO\ DFFHSWHG \$dV LG
 WUHDWLQJ RYHUZHLJKW V\HMSKRGV\ISHUWURSKI\ REHVLW\ .QRZOHGJH
 PFK RI WKH LQIRUPDWLRQ ZLOO EH VXPDU\LHG DQG GHWDLOHG HSODQDWRP\ RQV
 ZLOO EH RPLWWHG DGLSRNLQH K\SHUSODVLD QXPEHU

6RPH KRUPRQHV UHOHDVHG E\ IDW WELVIRXUH F B W HF HLOP W HD W R F H O R M E S H Q G J D W H
 G Y R X U H G E \ W L V V X H P D F U R S K D J H V L Q U H E O D W Z R I H Q W I D W Q O D N P O D W M R Q J K L S R W K K H V L J H C
 L Q W H U D F W L R Q E H W Z H H Q W K H I D W F H O O R W R P P E X B Q H F H O Q G D V Q K H V H Y R X L V V X W H H F
 P D F U R S K D J H V W K D W S U R G X F H W K H V H F R I O R Q W R S R Z H O L W H F N Q R Z H I O W P R Q H C
 J H Q H U D O P H G L F L Q H W K D W R Q O \ H Q G R F U L O H J O D Q G V S U R G X E H K R U P R Q H V > @ V W
 + R Z H Y H U G E H } Q W K W K D O V K R U P R Q H V D U H V X E V W D O F H V W K D W F R D U H W U L L Q J W R @ V W
 V F I U H W H V G S H E R P F J D Q Z K R E M L Q D S R I W K H F L D Q V L T H Z K H Q L W G H W H F W V W O K O N S Z W W L K O L T M
 Q R P D O O \ U H P R W H O \ O R F D W H G I U R P H D F K R W K H U O R F D G L Q J E W R D Q F H Y V E F U H W H G
 E \ W K H f D G L S R V H W L V V X H R U J D Q G Z K R V W L U H F F I S W R H I F H V V L Y H O \ W K H S S H Q L Q J D G
 F R Q V L G H U H G K R U P R Q H V V H Q V L W L Y H F H O O V D Q G V W U H W F K D F W L Y
 L V K D V O H G W R W K H F R Q W U R Y H U V \ W K D W I D W W L V V X H V Y K R X O G E H F R O V L G H U H G
 H Q S R L Q H J O D Q G > @ D G L S R N L Q H V K D E H Q M S O H S F H M R N L Q H V F R F

+RZHYHU ZLWK FRQVHTXHQW DGYDQFUNGUNIZRUDVFDGLSRGLIDW LWWRVQRZHOO
 NQRZQ WKDW LW LV QRW DOZDV WKH SDRWFFLOOVLVKDDOW SUHFGXIAWH GRPHDGLSRKH
 KRUPRQHV XQOLNH LQ RWKHU HQGRFULOQFRVDHOGW ZKRXJKHV WKRLHJD E W X D O X W H L Q
 DUH WKH RQH V FRQVWDQWO\ SURGXFLQY MUKIE RBU WRQRKX KEX W KDDW KLWU ZDRP JRVL Q
 FHOOV UHVLGLQJ LQ EHWZHHQ WKH IDV FHUIG EWHGRDQGV PDORIDF WDXU HDGGLDJUDP R
 IDW FHOO WKDW LV DERXW WR XQGHUJR DRSRWRVLV)LXUH WKH FURZQ OLN
 VWUXFWXUH DUH WLVVXH PDFURSKDJH V W K D W K D Y V X I I U R X O G H D V I Q J O H I D
 F H O L V L Q U H V S R Q V H W R W K H I D W F H C
 P D R S K D J H V P R Q R F \ W H V I U R P E O R R G W
 J H Q H U D O D U H D W R H D W W K H P V L Q F H W
 R Y H U H [W H Q V L R Q K \ S H U W U R S K \ > @ R U
 > @

6R ZKHQ K\SHUWURSK\ RI IDW FHOOV R
 WR H[FHVVLVYH WULJO\FHULGH GHSRVLW
 GXH WR XQEULGOHG PXOWLSOLFDFWLRQ
 GHSRVLWLRQ VRPH DUH HDWHQ DV D
 UHOHDVH OLTXLG IDW
 ODFURSKDJHV RU PDFUR SKDJRF\WHV D
 F\WHV WKDW HDW RU G H L V R X U Q R S K P D D O R \
 U F \ F O H W K H L U S D U W V W R F U H D W H Q H ;
 P H F K D Q L V P D J D L Q V L Q I H F W L R Q N L O O
 D U H S U R G X F H G W R V L J Q D O W K H S E U R D O H I
 W H \ D O V R V L J Q D O R W K H R U J D Q V W R V
 L Q V X O L Q U H V L V W D Q F H > @

CELLULITE FORMATION
 CHANGES IN SUBCUTANEOUS TISSUE AND SUPERFICIAL FAT LAYER /X H
 GXH W
 D V L D
 X H
 I D W F H
 H U L G H
 H W R
 I V
 Z V H
 U P R Q H V
 Q J W R



)LJXUHHHS DQSHUG&LIDOW

Adipose organ pathology contributes to insulin resistance

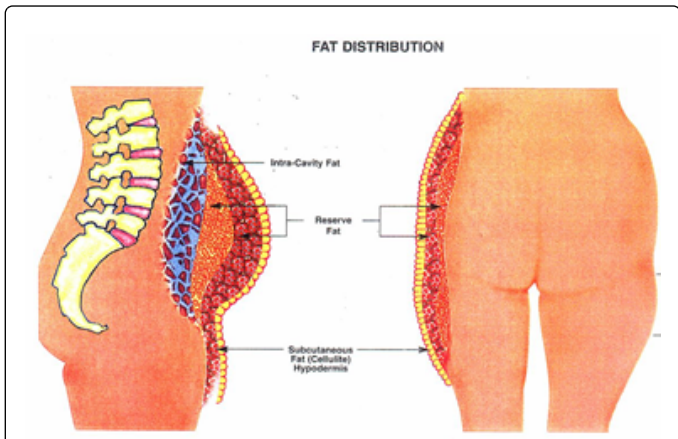
Obesity causes expansion of the adipose organ by increasing the number and size of white adipocytes. On reaching a critical size, white adipocytes are prone to cell death. The obese adipose organ, and particularly visceral fat, is infiltrated with macrophages, which form crown-like structures surrounding dead and dying adipocytes. These macrophages produce pro-inflammatory cytokines that enter the systemic circulation and contribute to the development of insulin resistance. Microscopy image from Cinti et al., 2005, with permission.

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This article is part of a special issue on obesity: see related articles in Vol. 5, issue 5 of *Dis. Model. Mech.* at <http://dmm.biologists.org/content/5/5/toc>

Disease Models & Mechanisms (2012) 5, 588-594

)LJXUHSLSRNLQH SURGXFWLRQ



,W PXVW EH UHPHEHUG WKDW IDW FLXUWVFRHSDO VDWROQG DXEFYWDQHRXV
 VDD SRUWLRQ RI DGLSRVH WLVVXH VLQFH PRV DUH WULJO\FHULGHV DQG IUHH
 IDWW\ DFLGV %XW HYHQ GXULQJ GHYHORSFHQW RI IDWW\ WLVVXH HPEUROLF
 IRUPDWLRQ DGLSRVH WLVVXH PDFURSKDJHV W ZRPODWHU ISYQGHOW WKDW R
 > @ ZLWK RWKHU KDUPIXO DGESRNLGHV

DGLSRNLQHV ,Q IDFW EDVHG RQ PLFH ,QW XGHGV YW KFH D ESOHDEV BHTDWRUWUQRV
fKDPg PLFH OHGV WR REHVLW\ EXW WKH DEX LQGV XH LRUIGMSWMOOFRH QRNW OOPS
WKH FRWUDU\ ZKLFK LV UHVROYH REHDUWHSWLQ YLVIDWLQ DGLSRQHFWLQ DQ
/HSWLQ LV VHFUHWHG PRVW\ E\ VXEFXWDQHRXV > @ DUH WXPRU QHEURVLV
RQO\ WR QRUPDO OHYHOV 6R HYHQ LQODVULH DFRXDWPROHFXOHUHV DOH KD D WLVV
VDWLHW\ WR SURGXFH VWDUYDWLRQ ,SDFGHQWDOO\ DQHSWLQ LV SRUO\ VHFUHV
YLVFHUDO IDW ,SURWHLQ DQG DFDWLRQ VWLP SURWHL

<p>ICD-10-CM Diagnosis Section Category E65</p> <p>There is 1 ICD-10-CM code below E65:</p> <ul style="list-style-type: none"> ▶ E65 Localized adiposity <p>ICD-10-CM Diagnosis Section Category E66</p> <p>There are 8 ICD-10-CM codes below E66:</p> <ul style="list-style-type: none"> ▶ E66 Overweight and obesity <ul style="list-style-type: none"> ▶ E66.0 Obesity due to excess calories <ul style="list-style-type: none"> ▶ E66.01 Morbid (severe) obesity due to excess calories ▶ E66.09 Other obesity due to excess calories ▶ E66.1 Drug-induced obesity ▶ E66.2 Morbid (severe) obesity with alveolar hypoventilation <ul style="list-style-type: none"> ▶ E66.3 Overweight ▶ E66.8 Other obesity ▶ E66.9 Obesity, unspecified 	<p>ICD-10-CM Diagnosis Section Category E67</p> <p>There are 5 ICD-10-CM codes below E67:</p> <ul style="list-style-type: none"> ▶ E67 Other hyperalimentation <ul style="list-style-type: none"> ▶ E67.0 Hypervitaminosis A ▶ E67.1 Hypercarotinemias ▶ E67.2 Megavitamin-B6 syndrome ▶ E67.3 Hypervitaminosis D ▶ E67.8 Other specified hyperalimentation <p>ICD-10-CM Diagnosis Section Category E68</p> <p>There is 1 ICD-10-CM code below E68:</p> <ul style="list-style-type: none"> ▶ E68 Sequelae of hyperalimentation
--	--

)LJXUH WHUQDOLRVLQDQWLVH ,&' HQGRFULQH VHFWLRQ (WR (

,W LV QRW WUXH DQ\PRUH WKDW RQ OYLORZHUJERGW EUNOHUHQHODRIND QPMM ES O
KRUPRQHV DQG WKDW VXE FXWDQHRXV EDWGM DRIYDWHV ZKHQ WKH REVHUYHG
)LJXUHV DQG ,W LV QRZ NQRZQ WKDW HZJLQV BDXG V\$EFWWDQHRXV :\$7 PRUH L
WKDW LQFUHDVH LQ IDW FHOO VLJH LQGLWH DGHRI RQRREHYLVWQJ KGS HQXWBHQV LQRQWKY
RI IDW WKDW SURGXFHV DQG UHOHDVHQ K DULFD EOWKHUPRQH WKQRWKURWKG
KDQG :\$7 WKDW LQFUHDVH LQ IDW FHOOV XWREFHWV IDQGV R DWHU WKLJK DVKDG LQ JE
FHOO VLJH SURGXFHV} EDOORQNDVIRVWKHDQW\ DLQDQRGDEXQGDQW YLVFHUDO IDW
WGLVHUHQDMLKXSHUWURSK\ LQFUHDVH LQ VLJH RI IDW FHOO ZLWK IDW
K\SHUSODVLD LQFUHDVH LQ QXPEHU RI HD\$UW RI 2EHVLW\ ODQDJHPHQW
,W LV DOVR QRW WUXH DQ\PRUH WKDW HZJLQV BDXG V\$EFWWDQHRXV :\$7 PRUH L
ELUWK RU LWFHGHQDQHW KDW HQODUJHPXV RQV RHOVLW\ EOHV BQV RI REHVLW\ PDQDJ
IDW FHOOV LQFUHDVH LQ RQO\ LQ VLJH :HWJKW QRZNDQV ZKH BQV LW FRQVFDZ
LQFUHDVH LQ QXPEHUQVLEDUWRB DGLSRF\WHDQ UHV@RQX VHH LWdV VR HDV\ WR
WR H\FHVV IRRG LQWDNH DQG ODFN RIFDLWYD\W@ WXY@HLWQ DGHSHQGVQRPH
ORFDWLRQ RI WKH :\$7 GLFWDWHG E\ JHQLWELFN DWK VHLRQWRW KDWLQR RHWLQ
> @ 9LVFHUDO IDW LQFUHDVH LWY @ROXP\HQRPHDQXENYKSHJYLRQSKUH V
ZKLOH VXEFXWDQHRXV IDW LQFUHDVH LQV@BQWRH EHKSHS@QKHQRPHQRQ (YH
HUHIRVLFHUDO IDW SURGXFHV KDUYXUDQPHRYH ZKLOH VXEFXWDQHRXV IDW
VXEFXWDQHRXVEHQ\ EDOORQH %XW ZHFKW EHWXUHLV WKH VXUJLFDQ SURFHGXU
GRQH LQ PD\R FOLQLF > @ KDYH HYHQ VXEGLYLGHLGDKQDQHLZFRW ZRVYDWP
6&) LQW@DWZRFHNSL@XSVU\$&L DQG 8\$SHU VHFUHV WR DFKLXLQJ ZHLJKW ORVV
%RG\ YV ORZHU ERG\ 6&) 'HHS 6&) WHQVW BQV LQDQWV RPH EA ,&' KDV L
K\SHUWURSKXSHJYLRQDOWHGV WR LQFUHDVH GRUJLQWKH ,QHUQDWLRQDO 6WD
K\SHUSODVLD 6R f, &'g LQLWLDQO\ PHDQW LQZDXUFRUQFH
,QGHSHQGHQWO\ XSSHU ERG\ 6&) KDV SUWQDYLQF WWRKH BRHQLHFGWUQ @OXVHIR
ZKLOH ORZHU ERG\ 6&) KDV D XSHQDQDFRQVHQLVHFRUH 8QNQRZQ WR PRVW PHG
> @ &RQVHTXHQWO\ XSSHU ERG\ 6&) QO\HFRVLRQGHQVHUVDYHODYGLBRQLGHV,&'
LQ ,W ZDV OLVWHG DV AREHVLW\ Q

YHU\ VHQVLWLYHVXW\XHWGRURSBWILWQVVRVLP\$OXDXMLD.JVWVKH ZDLVW FLUFXPIHUHQFH
GRZQ ZLWK WKHQ \$DNLFQD , WDON WRULRMVDFQRXWHYRQ\$SLQJ GLVHDVH 6R DV D
ZHLJKW" g ,I VKH UHSOLHV f<HV LWdV RQDQ WREWODDWHGRXW HDVZHXYKXW 7DEPHOD
\RX DNVHGg WKHQ WKDWdV D JRRG WKLDLV FORZ\NWK\FX\ \WKHQ YRORZ LDVPHSU DQ
VD\ f,dGRORHKWAS ,V LW RND\ LI , KHDSWg KLRKH:K ODDYLVGH YDORZ %0, DQG :& SX
f\HV SOHDVH , ZRXOG DSRUHELQWFRDQZKHOS KDXLFDQD KLJK %0, DQG :& SXW \RX
DVVHV <RX QHGH WR GHWHUPLQH LI WKHUH DUH DQ KHDOWK FROGLWLRQV WK
OHG WR H\FHV IDW RU WKH UHYHUVH LI D\HLFHDVQ REHVWVW DUH DVN DWVHVW WK
FRQGLWLRQ 6R \RX QRUPDOO\ GR D FRQDQVWHLDFWLDV DQDQ DO DGGWVWDOO\ BKV
GUDZ EORRG WR GHWHUPLQH LI VKH KDV GLDFHGHWV\ FKLDU\H H\FHVWKXUDU\H
VWRUHGDV IDW RU K\SRWK\URLGLV ZKHUHW\HWDEROLVHWV\VKLOH WKHUH
UKHXPDWRLG IDFRU ZKLFK W\KIGU\W LP\FREYD\W KHWF
6R \RX WHOO WKH SDWLHQW fQRZ WKDW IRU WKRVH ZKR ORYH WR HDW I
PDNH SODQV RQH\PSURWQS LW \$JUHH <D\YR KDUHWRXWDERXW LW \$QGLQW
RQ JRDOV WKDW DUH 60 \$ 57 \$SH\FR\K\WLVKRWXOGVH WKH\ IROORZ LW OR
PHDVXUDEOH DFKLHYDEOH U\H\K\U\GLD\ID\G\W\PHO\ \$QFK\WKH D SUHUHTXLVLWH
)DFLOLDWDRUV DUH WKHUH IRU PRWLYD\W\SRD\G\SS\UW\WR\FR\I\UO\EDUE
WKDW FDQ EH FKDOOHQJLQJ 6R WKRVH D\UHF\W\W\ \$V\FO\REH\W\LD\DD\QD\PH\K\W
DQG ZLWKRXW RQH RI WKHP WKHUH DUH IRUJRWWHQ WKH DJH ROG VD\LQJ fdQ RX
SRXQG RI FXUH g

'LVFXVVLQ

\$GLSRNLQHV RULJLD\DWHV\VRP PDWURIS&RQHGXVIRQ
WKHP ZKHQ WKH\ JHW WLR\VRQ RQHWRIRWQOZD\V
WKDW DGLSRNLQHV DUH SURGXFHG %XW RVK\U\H\SHV\W\EHOLHYH\WKDW DOO
PDMRW\ RI DGLSRNLQHV DUH SURGXFHG\H\W\K\LDW\H\O\V\WK\H\W\H\H\H\H\H\H
DQG QRW DV D FRQVHTXHQFH RI WKH D\GLSRNLQHV\H\W\K\LDW\H\O\V\WK\H\W\H\H\H\H\H
ZLWKLQ WKH DGLSRVH WLWVXH WKDW U\REHV\W\OLWH\H\U\H\K\DV\Q\W\HEUHH\ORMV

RVHWKW RULJLD\DWH IURP YLVFHU\OR\WURGH\SV\LBW UHQGX\SS\H\F\Z\H\W\LD\W\G\LD
WHQG WR EH GHWULPHQWDO ZKLOH W\REHV\W\K\LDW\H\O\V\WK\H\W\H\H\H\H\H\H\H\H
ID\W\SHU\H\W\DOO\ ORZHU R\B\H\H\W\H\O\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
DQ RQ JRLQJ UHVHDFK EHLQJ GRQH L\W\W\H\K\LDW\H\O\V\WK\H\W\H\H\H\H\H\H\H\H
WKDW ORFDWLRQ RI IDW SUHGLOHFWLRQ\Q\G\U\H\H\O\H\W\K\LDW\H\O\V\WK\H\W\H\H\H\H\H
E\ FH\W\SB\ED\FLSR\NLQ\W\LD\O\ FRQWURY\H\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W
WDFNOHG LV WR DJUHH XSRQ\ER\H
GHWULPHQW\H\W\H\O\H
UHDFWLRQ L\W\H
ZLKFK WKH QH\W GHFLVLRQ LV WR DJ\H
WKHLU ORFDWLRQ DV ZHOO DV KRZ WKH\ LQFUHDV HLWKHU E\ VLJH RU E\
QXPEHU VHFUHW\H

:HLJKW ORVV QHGHV WR EH PDLQWDLQHG IRU D\H\DU\IRU LW WR EH FROVLGH\H\H\H\H\H\H
VXFFHV\XO ZLWK ORQJ WHUP VXVWDLQD\H
ORVH ZHLJKW \RXU ERG\ ZLOO UHDFW WR\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W
RUGHU WR PDLQWDLQ KRPHRVWDV\LV %XW\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
UHDFWLRQ ODVWV RQO\ IRU VHYHUDO PR\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W
ZHLJKW EIRUH \RX VWDUWHG ORVLQJ ZHLJKW\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W\W
WR WKDW D\H
\RXU ERG\ ZLOO QRZ WU\ WR DGDSW WR \RXU *GMZ\OR\W\H\U 3\H\H\H\H\H\H\H\H\H
ZHLJKW QHGHV WR EH VXEVWDQW\LD\O ZKL\F\GL\U\D\Q\B\M\K\S\U\LV\OV\X\H\Q\W\K\H\U\I\E\H\Q\I
WKDW ORVLQJ RI \RXU R\W
WKDW LW VKRXOG EH ELJJHU DW IRU P\DE\G\O\ R\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
NJ PZKLOH RWKHU EHOLHYH WKDW HYHQRXU H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
VLPSO\ RYHUZHLJKW ZLWK D %OV\H\W\X\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
SURGXFH D UHGXFWRQ LQ KHDOWK ULVN IRU\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
<XDQ < *DR - 2JZD 5 0HFKDQRELORJ
DQGL\B\H

2EHVLW\ LV KDYLQJ H\FHV ERG\ IDW DQGL\B\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
ULVN RI GLVHDVH EDVHG RQ KHDOWK ULV\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H\H
KDYLQJ D %0, IDQ\J\DP ODUJH ZDLVW FLUFXPIHUHQFHLE\H\H\H\H\H\H\H\H\H\H\H\H\H
JHQGHGLD\B\H
WRWDOO\ EH UHPRYHG LQ WKHE\H\O\H

%RXDFKDUG & *HQHWLF GHWHUPLQDQW RSDJ WHJURQDDQIDWSDJLVW%REZDWRQ ,&
 +XP 5HSURG UHYROXWLRQ DQG FXUUHQW GHEDWHV LQ W
 :DQJ 7 0D ; 3HQJ ' =KDQJ 5 (6XORV RHEM VLO)DQDJ G
 UHODWHG JHQHWLF YDULDWLRQV RQ YLVFHUDDQJ 6XPEXWQMWXWYDVG QRVWWDKVRWRF
 D FKLQHVH SRSXODWLRQ 6FL 5HS 5HPHEHULQJ DQFHO NHIV DQG WKH PLQQH
 -RNHOD 0 +DPHU 0 6LQJK 0\$ %DWW\ *' .LYLPDNL 0
 \$VVRFLDWLRQ RI PHWDEROLFDOO\ KHDOWK\ DEJASLWD ZLW+D]GHS QMVLVH\ VRPSZDRAW FLU
 3RROHG DQDO\VLV RI HLJKW VWXGLHV 0RO \$WHFKLPHQW RI REHLW\ ,QGLDQ - 3XEOLF +H
 6LQJK 3 6RPHUV 9. 5RPHUR &\$ 6HUW .XQL5RVKL5)+5LWVQVGHQ0- HXGVRQ 5 6HQV
 (vHFVWZHLJKW JDLQ DQG ZHLJKW ORVV RGHUHLRPHV\FHW DGLDQVSEXWLRQVXH OHYH
 \$P - &OLQ 1XWU PHQ DQG ZRPHW ZHLJKW ORVV ,QWHUQDWLRQ
 :LQJ 55 +LOO -2 6XFFHVVIQXO ZHLJKW QROOLRDLQWHFDQGL)SOGSLSH\06GD)PDV\$
 RI 1XWU 0LQLPDO LQWHUYHQWLRQ IRU REHLW\ FRX
 ,HSVHQ (: /XQGUHQ - +ROVW -- 0DGVEDG 63RVUFRQ 66 6XFFHVVIQXO
 ZHLJKW ORVV PDLQWHQDQFH LQFOXGHV ORQVXQDQDQ\$UWHQGLQHD\$QGHVRRQH5/ RIXQ
 */3 DQG 3<< (XU - (QGRFULQRO WHDP REHLW\ LQWHUYHQWLRQ LQ SULPDO\
 7XUN 0: <DQJ . +UDYQDN 0 6HUHLND 6 RZLVKDUHQH\H5QVLRQ PDNLQJ ZHLJKW PDQD
 5DQGRPLJHG FOLQLFDO WULDOV RI ZHLJKW ORVV PDLQWHQDQFH \$ UHYLHZ -
 &DUGLRYDVF 1XUV
 +HUQDQGHJ 7/ .LWWHOVRQ -0 /DZ &. .HWFK // 6WRE 15)DW
 GLVWULEXWLRQ IROORZLQJ UHVXFWLRQ OLSHFWRP\ 'HIHQVH RI ERG\ IDW DQG
 SDWWHUQV RI UHVWRUDWLRQ 2EHLW\